STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 195103

TO: CECILIA JAISLE
Location: REM/4E78/5C18
Art Unit: 1624
Wednesday, July 19, 2006
Case Serial Number: 10/533697

From: John DiNatale
Location: Biotech-Chem Library
REM-1B65
Phone: (571)272-2557

john.dinatale@uspto.gov

Search Notes

Examiner JAISLE,

See attached results.

If you have any questions about this search, or need assistance understanding the MARPAT indexing, feel free to contact me at any time.

Thank you for using STIC search services!

John DiNatale
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-2557

Search history


```
=> d his full

     (FILE 'HOME' ENTERED AT 10:16:46 ON 19 JUL 2006)

     FILE 'REGISTRY' ENTERED AT 10:16:52 ON 19 JUL 2006
L1             STRUCTURE UPLOADED
L2           2 SEA SSS SAM L1
               D SCA

     FILE 'STNGUIDE' ENTERED AT 10:18:18 ON 19 JUL 2006

     FILE 'STNGUIDE' ENTERED AT 10:21:32 ON 19 JUL 2006

     FILE 'REGISTRY' ENTERED AT 10:28:53 ON 19 JUL 2006
L3             STRUCTURE UPLOADED
L4           2 SEA SSS SAM L3
               D SCA

     FILE 'STNGUIDE' ENTERED AT 10:31:21 ON 19 JUL 2006

     FILE 'REGISTRY' ENTERED AT 10:31:53 ON 19 JUL 2006
L5             STRUCTURE UPLOADED
L6           2 SEA SSS SAM L5
               D SCA
L7          16 SEA SSS FUL L5
               SAVE TEMP L7 JAI697STRC/A
               D STAT QUE L6
               D STAT QUE L7
               D SCA L7

     FILE 'CAPLUS' ENTERED AT 10:36:35 ON 19 JUL 2006
L8           1 SEA ABB=ON  PLU=ON  L7

     FILE 'BEILSTEIN' ENTERED AT 10:37:03 ON 19 JUL 2006
L9           0 SEA SSS SAM L5
L10          0 SEA SSS FUL L5

     FILE 'MARPAT' ENTERED AT 10:37:35 ON 19 JUL 2006

     FILE 'CAPLUS' ENTERED AT 10:38:10 ON 19 JUL 2006
               E US2003-533697 /APPS
               E US2005-533697 /APPS
L11          1 SEA ABB=ON  PLU=ON  US2005-533697 /AP
               D SCA
               SEL RN

     FILE 'REGISTRY' ENTERED AT 10:39:21 ON 19 JUL 2006
L12         30 SEA ABB=ON  PLU=ON  (110-91-8/BI OR 16182-04-0/BI OR 5028-13-7/
               BI OR 6298-19-7/BI OR 663918-38-5/BI OR 684648-96-2/BI OR
               684648-97-3/BI OR 684648-98-4/BI OR 684648-99-5/BI OR 684649-00
               -1/BI OR 684649-01-2/BI OR 684649-02-3/BI OR 684649-03-4/BI OR
               684649-04-5/BI OR 684649-05-6/BI OR 684649-06-7/BI OR 684649-07
               -8/BI OR 684649-08-9/BI OR 684649-09-0/BI OR 684649-10-3/BI OR
               684649-11-4/BI OR 684649-12-5/BI OR 684649-13-6/BI OR 684649-14
               -7/BI OR 684649-15-8/BI OR 684649-16-9/BI OR 684649-17-0/BI OR
               684649-18-1/BI OR 684649-19-2/BI OR 684649-20-5/BI)
L13          14 SEA ABB=ON  PLU=ON  L12 NOT L7
               D SCA

     FILE 'STNGUIDE' ENTERED AT 10:41:13 ON 19 JUL 2006
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     FILE 'REGISTRY' ENTERED AT 10:44:06 ON 19 JUL 2006
L14             STRUCTURE UPLOADED
L15           3 SEA SSS SAM L14
                D SCA
L16          29 SEA SSS FUL L14
                SAVE TEMP L16 JAI697STRD/A
L17          13 SEA ABB=ON  PLU=ON  L16 NOT L7
                D SCA

     FILE 'CAPLUS' ENTERED AT 10:48:42 ON 19 JUL 2006
L18           3 SEA ABB=ON  PLU=ON  L17
L19           0 SEA ABB=ON  PLU=ON  L11 AND L18

     FILE 'BEILSTEIN' ENTERED AT 10:49:29 ON 19 JUL 2006
L20           0 SEA SSS SAM L14
L21           8 SEA SSS FUL L14
L22           1 SEA ABB=ON  PLU=ON  L21 NOT L18

     FILE 'REGISTRY' ENTERED AT 10:51:15 ON 19 JUL 2006
L23             ANALYZE PLU=ON  L16 1- LC :       5 TERMS
                D
L24           2 SEA ABB=ON  PLU=ON  L16 NOT CAPLUS/LC
                D SCA
L25           7 SEA ABB=ON  PLU=ON  L16 AND BEILSTEIN/LC
L26           0 SEA ABB=ON  PLU=ON  L24 AND L25
                D LC L24 1-2
                D SCA L24
                D ED L24 1-2
                D COST

     FILE 'MARPAT' ENTERED AT 10:55:02 ON 19 JUL 2006
L27           1 SEA SSS SAM L14
L28          49 SEA SSS FUL L14
                SAVE TEMP L28 JAI697MARPD/A
L29           1 SEA SUB=L28 SSS SAM L5
L30          24 SEA SUB=L28 SSS FUL L5

     FILE 'CAPLUS' ENTERED AT 11:01:21 ON 19 JUL 2006
L31          24 SEA ABB=ON  PLU=ON  L30
L32           1 SEA ABB=ON  PLU=ON  L18 AND L31
L33           0 SEA ABB=ON  PLU=ON  L18 AND L8

     FILE 'WPIX' ENTERED AT 11:02:47 ON 19 JUL 2006
L34           1 SEA SSS SAM L14
                D SCA
L35          16 SEA SSS FUL L14
                D SCA

     FILE 'STNGUIDE' ENTERED AT 11:04:04 ON 19 JUL 2006

     FILE 'WPIX' ENTERED AT 11:04:29 ON 19 JUL 2006
L36           2 SEA ABB=ON  PLU=ON  L35/DCR
                SEL SDCN L35
                EDIT E31-E46 /SDCN /DCN
L37           2 SEA ABB=ON  PLU=ON  (RAEA00/DCN OR RAEA01/DCN OR RAEA02/DCN OR
                RAEA03/DCN OR RAEA04/DCN OR RAEA05/DCN OR RAEA07/DCN OR
                RAEA08/DCN OR RAE9ZS/DCN OR RAE9ZT/DCN OR RAE9ZU/DCN OR
                RAE9ZV/DCN OR RAE9ZW/DCN OR RAE9ZX/DCN OR RAE9ZY/DCN OR
                RAFSCY/DCN)
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                SEL DCSE L35
                EDIT E47-E62 /DCSE /DCRE
L38           2 SEA ABB=ON  PLU=ON  (902542-0-0-0/DCRE OR 902543-0-0-0/DCRE OR
                902544-1-0-0/DCRE OR 902544-2-0-0/DCRE OR 902546-0-0-0/DCRE OR
                902547-0-0-0/DCRE OR 902548-1-0-0/DCRE OR 902548-2-0-0/DCRE OR
                902550-1-0-0/DCRE OR 902551-0-0-0/DCRE OR 902552-1-0-0/DCRE OR
                902552-2-0-0/DCRE OR 902553-0-0-0/DCRE OR 902557-0-0-0/DCRE OR
                902558-0-0-0/DCRE OR 976436-1-0-0/DCRE)
L39           2 SEA ABB=ON  PLU=ON  (L36 OR L37 OR L38)

     FILE 'STNGUIDE' ENTERED AT 11:07:27 ON 19 JUL 2006

     FILE 'CAPLUS' ENTERED AT 11:07:54 ON 19 JUL 2006
L40           4 SEA ABB=ON  PLU=ON  L16

     FILE 'BABS' ENTERED AT 11:08:44 ON 19 JUL 2006

     FILE 'BEILSTEIN' ENTERED AT 11:09:10 ON 19 JUL 2006
                SEL BABSAN L21

     FILE 'BABS' ENTERED AT 11:09:30 ON 19 JUL 2006
L41           1 SEA ABB=ON  PLU=ON  5564377/BABSAN

     FILE 'CAPLUS' ENTERED AT 11:10:41 ON 19 JUL 2006

     FILE 'HCAPLUS' ENTERED AT 11:11:51 ON 19 JUL 2006
L42           4 SEA ABB=ON  PLU=ON  L16
L43         275 SEA ABB=ON  PLU=ON  RAULT S?/AU
L44         256 SEA ABB=ON  PLU=ON  LANCELOT J?/AU
L45         212 SEA ABB=ON  PLU=ON  KOPP M?/AU
L46         121 SEA ABB=ON  PLU=ON  CAIGNARD D?/AU
L47         516 SEA ABB=ON  PLU=ON  PFEIFFER B?/AU
L*** DEL    107 S RENARD P//AU
L48         511 SEA ABB=ON  PLU=ON  RENARD P?/AU
L49           2 SEA ABB=ON  PLU=ON  L43 AND L44 AND L45 AND L46 AND L47 AND
                L48
L50          86 SEA ABB=ON  PLU=ON  L43 AND (L44 OR L45 OR L46 OR L47 OR L48)
L51          14 SEA ABB=ON  PLU=ON  L44 AND (L45 OR L46 OR L47 OR L48)
L52           4 SEA ABB=ON  PLU=ON  L45 AND (L46 OR L47 OR L48)
L53          91 SEA ABB=ON  PLU=ON  L46 AND (L47 OR L48)
L54         128 SEA ABB=ON  PLU=ON  L47 AND L48
L55         269 SEA ABB=ON  PLU=ON  (L50 OR L51 OR L52 OR L53 OR L54)
L56          21 SEA ABB=ON  PLU=ON  L50 AND (L51 OR L52 OR L53 OR L54)
L57          10 SEA ABB=ON  PLU=ON  L51 AND (L52 OR L53 OR L54)
L58           4 SEA ABB=ON  PLU=ON  L52 AND (L53 OR L54)
L59          21 SEA ABB=ON  PLU=ON  (L56 OR L57 OR L58)

     FILE 'MARPAT' ENTERED AT 11:16:14 ON 19 JUL 2006

     FILE 'HCAPLUS' ENTERED AT 11:16:28 ON 19 JUL 2006
L60           1 SEA ABB=ON  PLU=ON  L59 AND L42

     FILE 'MARPAT' ENTERED AT 11:16:43 ON 19 JUL 2006

     FILE 'HCAPLUS' ENTERED AT 11:16:54 ON 19 JUL 2006
L61           1 SEA ABB=ON  PLU=ON  (L43 OR L44 OR L45 OR L46 OR L47 OR L48)
                AND L42

     FILE 'MARPAT' ENTERED AT 11:17:33 ON 19 JUL 2006
L62          21 SEA ABB=ON  PLU=ON  L43
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L63          14 SEA ABB=ON  PLU=ON  L44
L64           4 SEA ABB=ON  PLU=ON  L45
L65          55 SEA ABB=ON  PLU=ON  L46
L66          41 SEA ABB=ON  PLU=ON  L47
L67         134 SEA ABB=ON  PLU=ON  L48
L68           1 SEA ABB=ON  PLU=ON  (L62 OR L63 OR L64 OR L65 OR L66 OR L67)
                AND L30

     FILE 'WPIX' ENTERED AT 11:18:26 ON 19 JUL 2006
L69          26 SEA ABB=ON  PLU=ON  RAULT S?/AU
L70          22 SEA ABB=ON  PLU=ON  LANCELOT J?/AU
L71          54 SEA ABB=ON  PLU=ON  KOPP M?/AU
L72          58 SEA ABB=ON  PLU=ON  CAIGNARD D?/AU
L73         128 SEA ABB=ON  PLU=ON  PFEIFFER B?/AU
L74         239 SEA ABB=ON  PLU=ON  RENARD P?/AU
L75           1 SEA ABB=ON  PLU=ON  L39 AND (L69 OR L70 OR L71 OR L72 OR L73
                OR L74)
L76          91 SEA ABB=ON  PLU=ON  (L50 OR L51 OR L52 OR L53 OR L54)
L77          10 SEA ABB=ON  PLU=ON  (L56 OR L57 OR L58)

     FILE 'STNGUIDE' ENTERED AT 11:20:11 ON 19 JUL 2006

     FILE 'WPIX' ENTERED AT 11:20:34 ON 19 JUL 2006
L78           1 SEA ABB=ON  PLU=ON  L77 AND L39

     FILE 'STNGUIDE' ENTERED AT 11:20:46 ON 19 JUL 2006

     FILE 'REGISTRY' ENTERED AT 11:22:09 ON 19 JUL 2006
                D STAT QUE L16

     FILE 'HCAPLUS' ENTERED AT 11:22:23 ON 19 JUL 2006
                D QUE NOS L59
                D QUE NOS L61
L79          21 SEA ABB=ON  PLU=ON  L59 OR L61

     FILE 'MARPAT' ENTERED AT 11:23:27 ON 19 JUL 2006
                D QUE NOS L68

     FILE 'WPIX' ENTERED AT 11:23:55 ON 19 JUL 2006
                D QUE NOS L78
                D QUE NOS L77
                D QUE NOS L75
L80          10 SEA ABB=ON  PLU=ON  L78 OR L77 OR L75

     FILE 'STNGUIDE' ENTERED AT 11:25:19 ON 19 JUL 2006

     FILE 'HCAPLUS, WPIX, MARPAT' ENTERED AT 11:25:45 ON 19 JUL 2006
L81          23 DUP REM L79 L80 L68 (9 DUPLICATES REMOVED)
                     ANSWERS '1-21' FROM FILE HCAPLUS
                     ANSWERS '22-23' FROM FILE WPIX
                D IBIB ABS HITSTR L81 1-23

     FILE 'STNGUIDE' ENTERED AT 11:27:06 ON 19 JUL 2006

     FILE 'REGISTRY' ENTERED AT 11:27:26 ON 19 JUL 2006
                D STAT QUE L42
L82          29 SEA ABB=ON  PLU=ON  L42 NOT L79

     FILE 'STNGUIDE' ENTERED AT 11:28:34 ON 19 JUL 2006
                D COST
```

```
             D COST FULL

     FILE 'STNGUIDE' ENTERED AT 11:30:59 ON 19 JUL 2006

     FILE 'HCAPLUS' ENTERED AT 11:31:17 ON 19 JUL 2006
               D QUE NOS L42
L83            3 SEA ABB=ON  PLU=ON  L42 NOT L79

     FILE 'BABS' ENTERED AT 11:32:30 ON 19 JUL 2006
               D STAT QUE L41

     FILE 'BEILSTEIN' ENTERED AT 11:32:55 ON 19 JUL 2006
               D STAT QUE L22

     FILE 'WPIX' ENTERED AT 11:33:26 ON 19 JUL 2006
               D STAT QUE L39
L84            1 SEA ABB=ON  PLU=ON  L39 NOT L80

     FILE 'MARPAT' ENTERED AT 11:33:55 ON 19 JUL 2006
               D STAT QUE L30
L85           23 SEA ABB=ON  PLU=ON  L30 NOT L68

     FILE 'STNGUIDE' ENTERED AT 11:34:23 ON 19 JUL 2006

     FILE 'HCAPLUS, WPIX, BABS, MARPAT, BEILSTEIN' ENTERED AT 11:35:09 ON 19
     JUL 2006
L86           26 DUP REM L83 L84 L41 L85 L22 (3 DUPLICATES REMOVED)
                    ANSWERS '1-3' FROM FILE HCAPLUS
                    ANSWERS '4-25' FROM FILE MARPAT
                    ANSWER '26' FROM FILE BEILSTEIN
               D IBIB ABS HITSTR L86 1-3
               D IBIB ABS HIT L86 4-25
               D IDE ALLREF L86 26


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   18 JUL 2006  HIGHEST RN 894196-03-3
     DICTIONARY FILE UPDATES:  18 JUL 2006  HIGHEST RN 894196-03-3

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/ONLINE/UG/regprops.html

     FILE STNGUIDE
     FILE CONTAINS CURRENT INFORMATION.
```

LAST RELOADED: Jul 17, 2006 (20060717/UP).

FILE CAPLUS

FILE COVERS 1907 - 19 Jul 2006 VOL 145 ISS 4
FILE LAST UPDATED: 18 Jul 2006 (20060718/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

FILE BEILSTEIN
FILE LAST UPDATED ON JUNE 16, 2006

FILE COVERS 1771 TO 2006.
FILE CONTAINS 9,606,495 SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

****
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *
* FOR PRICE INFORMATION SEE HELP COST *
****

NEW

*** PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.**

*** NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.**

FILE MARPAT
FILE CONTENT: 1961-PRESENT VOL 145 ISS 1 (20060714/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 2006118302 08 JUN 2006
DE 102004053653 04 MAY 2006
EP 1653548 03 MAY 2006
JP 2006112980 27 APR 2006
WO 2006053912 26 MAY 2006
GB 2419594 03 MAY 2006
FR 2877004 28 APR 2006
RU 2275374 27 APR 2006
CA 2518664 10 MAR 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

FILE WPIX
FILE LAST UPDATED: 14 JUL 2006 <20060714/UP>
MOST RECENT DERWENT UPDATE: 200645 <200645/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS
INDEX ENHANCEMENTS PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

FILE BABS
FILE LAST UPDATED: 15 JUN 2006 <20060615/UP>
FILE COVERS 1980 TO DATE.

FILE HCAPLUS

FILE COVERS 1907 - 19 Jul 2006 VOL 145 ISS 4
FILE LAST UPDATED: 18 Jul 2006 (20060718/ED)

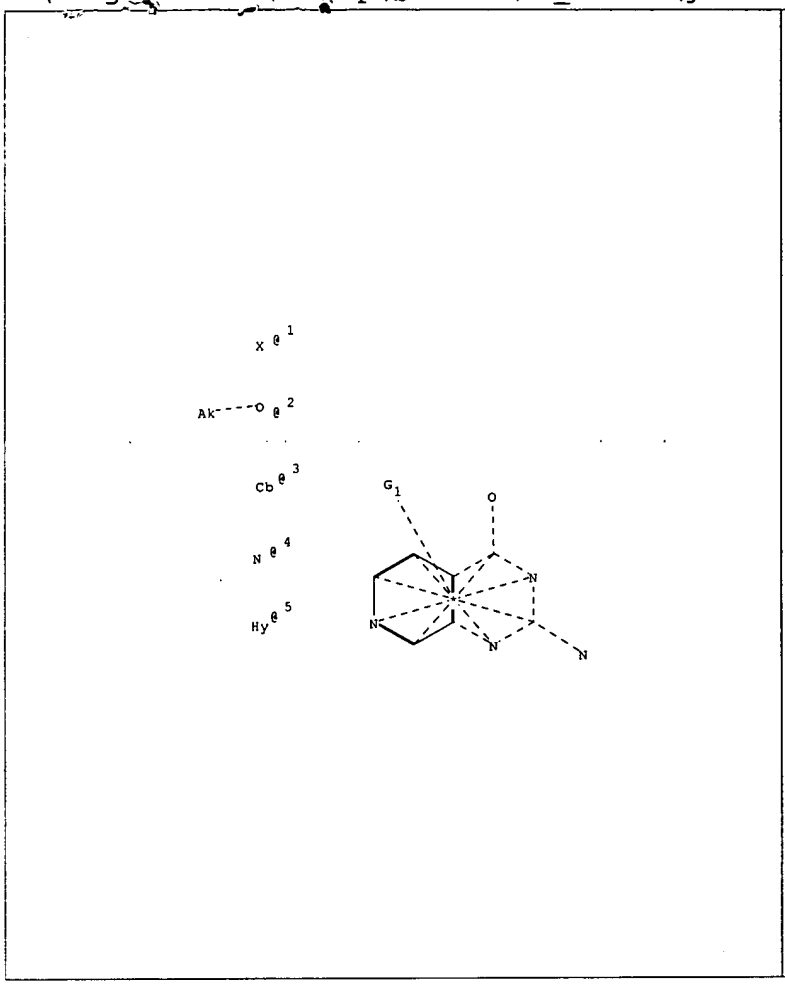
New CAS Information Use Policies, enter HELP USAGETERMS for details.

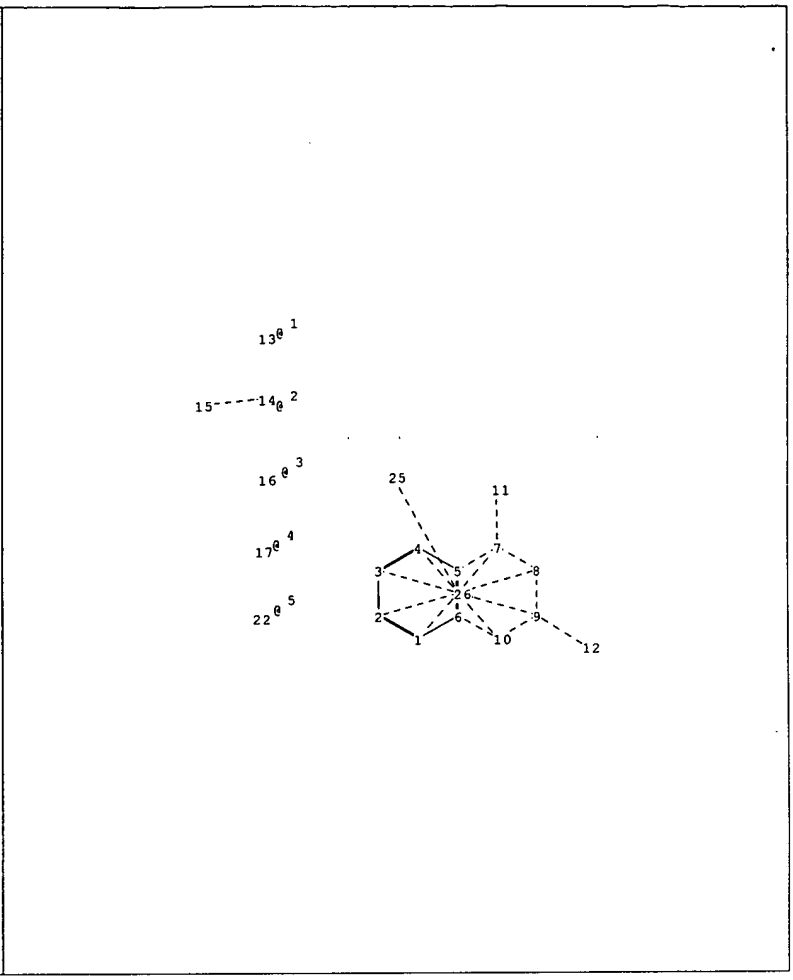
This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

C:\Program Files\Stnexp\Queries\10_533697\jaisle-c.str

structure "L5"





chain nodes :
11 13 14 15 16 22 25
ring nodes :
1 2 3 4 5 6 7 8 9 10
ring/chain nodes :
12 17
chain bonds :
7-11 9-12 14-15
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
exact/norm bonds :
5-7 6-10 7-8 7-11 8-9 9-10 9-12 14-15
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

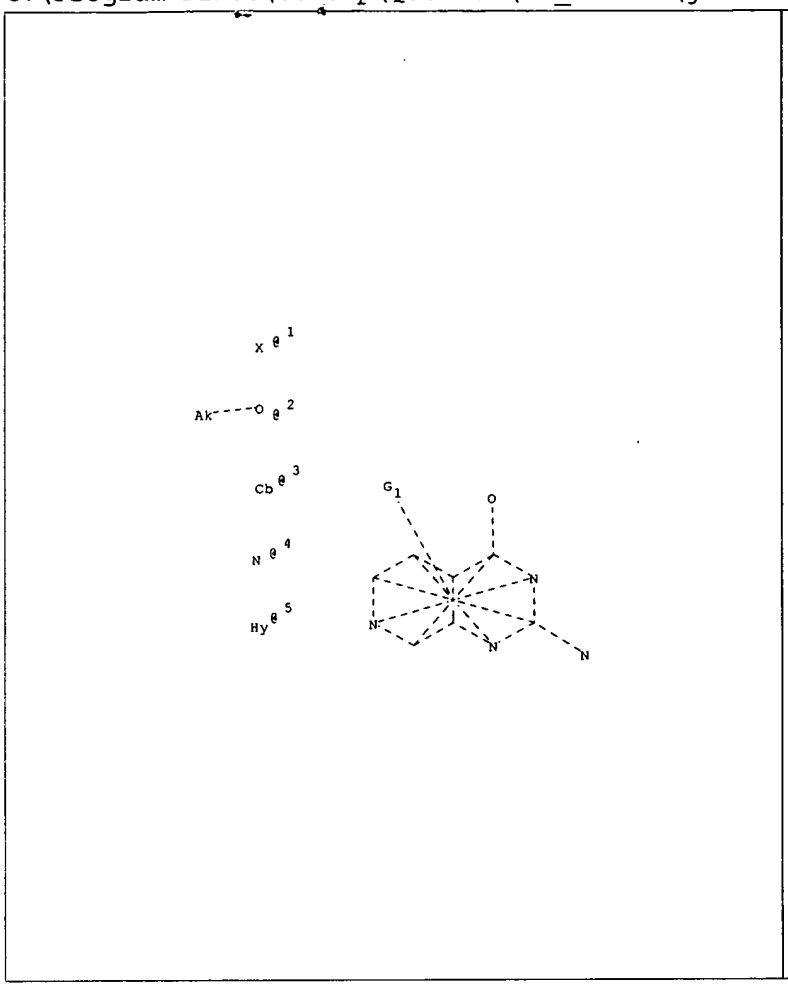
G1:[*1],[*2],[*3],[*4],[*5]

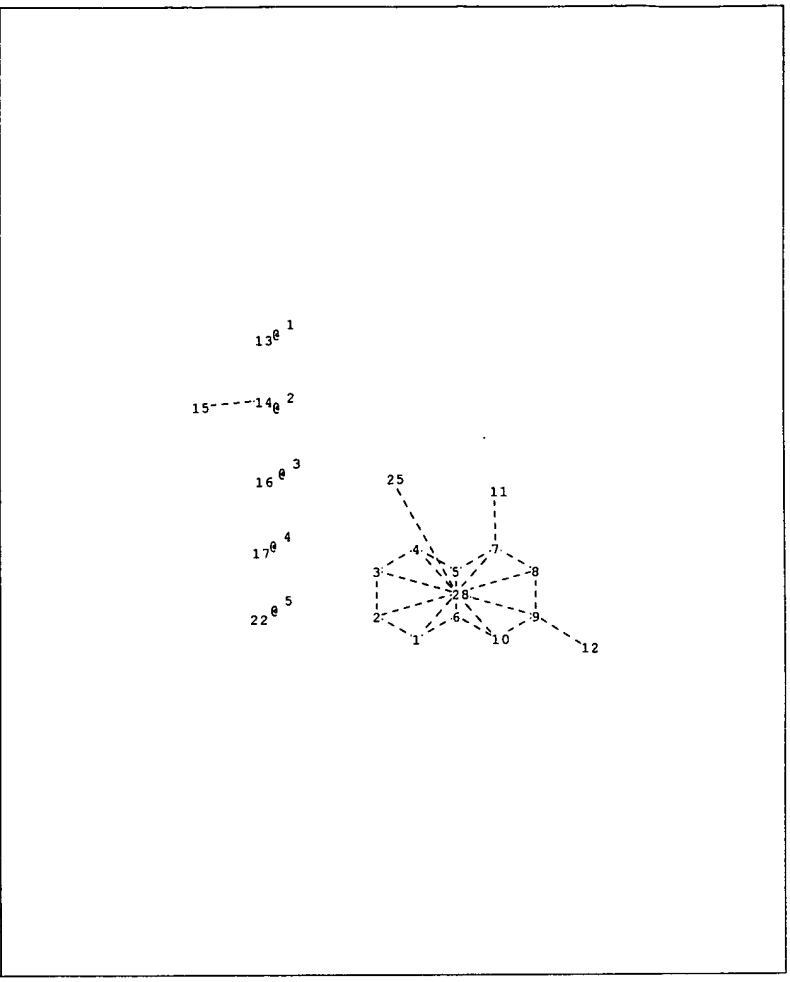
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 14:Atom 15:CLASS 16:CLASS 17:Atom 22:CLASS 25:CLASS 26:CLASS
Generic attributes :
16:
Saturation : Unsaturated

Element Count :
Node 22: Unlimited

C:\Program Files\Stnexp\Queries\10_533697\jaisle-d.str

structure "L14"





chain nodes :
11 13 14 15 16 22 25
ring nodes :
1 2 3 4 5 6 7 8 9 10
ring/chain nodes :
12 17
chain bonds :
7-11 9-12 14-15
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 9-10 9-12 14-15

G1:[*1],[*2],[*3],[*4],[*5]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 14:Atom 15:CLASS 16:CLASS 17:Atom 22:CLASS 25:CLASS 28:CLASS
Generic attributes :
16:
Saturation : Unsaturated

Element Count :
Node 22: Unlimited
N,N1

```
=> file registry
FILE 'REGISTRY' ENTERED AT 11:22:09 ON 19 JUL 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
```



```
Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    18 JUL 2006  HIGHEST RN 894196-03-3
DICTIONARY FILE UPDATES:   18 JUL 2006  HIGHEST RN 894196-03-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

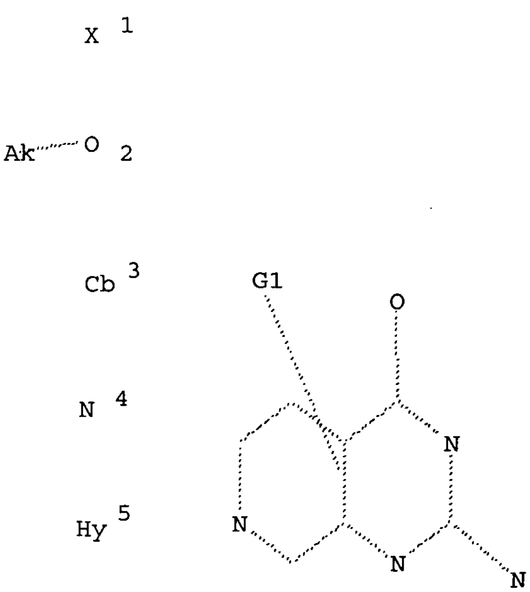
TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d stat que L16
L14                STR
```




```
G1 [@1],[@2],[@3],[@4],[@5]
```

STRUCTURE QUERY

```
Structure attributes must be viewed using STN Express query preparation.
L16            29 SEA FILE=REGISTRY SSS FUL L14

100.0% PROCESSED      712 ITERATIONS                       29 ANSWERS
SEARCH TIME: 00.00.01
```

```
=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 11:22:23 ON 19 JUL 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
```

AUTHOR SEARCH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FILE COVERS 1907 - 19 Jul 2006  VOL 145 ISS 4
FILE LAST UPDATED: 18 Jul 2006  (20060718/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que nos L59
L43          275 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RAULT S?/AU
L44          256 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LANCELOT J?/AU
L45          212 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KOPP M?/AU
L46          121 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CAIGNARD D?/AU
L47          516 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PFEIFFER B?/AU
L48          511 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RENARD P?/AU
L50           86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L43 AND (L44 OR L45 OR L46 OR
                 L47 OR L48)
L51           14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L44 AND (L45 OR L46 OR L47 OR
                 L48)
L52            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45 AND (L46 OR L47 OR L48)
L53           91 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L46 AND (L47 OR L48)
L54          128 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L47 AND L48
L56           21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L50 AND (L51 OR L52 OR L53 OR
                 L54)
L57           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND (L52 OR L53 OR L54)
L58            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L52 AND (L53 OR L54)
L59           21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L56 OR L57 OR L58)


=> d que nos L61
L14              STR
L16           29 SEA FILE=REGISTRY SSS FUL L14
L42            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16
L43          275 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RAULT S?/AU
L44          256 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LANCELOT J?/AU
L45          212 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KOPP M?/AU
L46          121 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CAIGNARD D?/AU
L47          516 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PFEIFFER B?/AU
L48          511 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RENARD P?/AU
L61            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L43 OR L44 OR L45 OR L46 OR
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```
              L47 OR L48) AND L42


=> s L59 or L61
L79         21 L59 OR L61

=> file marpat
FILE 'MARPAT' ENTERED AT 11:23:27 ON 19 JUL 2006
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FILE CONTENT: 1961-PRESENT VOL 145 ISS 1 (20060714/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US   2006118302 08 JUN 2006
DE 102004053653 04 MAY 2006
EP      1653548 03 MAY 2006
JP   2006112980 27 APR 2006
WO   2006053912 26 MAY 2006
GB      2419594 03 MAY 2006
FR      2877004 28 APR 2006
RU      2275374 27 APR 2006
CA      2518664 10 MAR 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.


=> d que nos L68
L5              STR
L14             STR
L28          49 SEA FILE=MARPAT SSS FUL L14
L30          24 SEA FILE=MARPAT SUB=L28 SSS FUL L5
L43         275 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RAULT S?/AU
L44         256 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LANCELOT J?/AU
L45         212 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KOPP M?/AU
L46         121 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CAIGNARD D?/AU
L47         516 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PFEIFFER B?/AU
L48         511 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RENARD P?/AU
L62          21 SEA FILE=MARPAT ABB=ON  PLU=ON  L43
L63          14 SEA FILE=MARPAT ABB=ON  PLU=ON  L44
L64           4 SEA FILE=MARPAT ABB=ON  PLU=ON  L45
L65          55 SEA FILE=MARPAT ABB=ON  PLU=ON  L46
L66          41 SEA FILE=MARPAT ABB=ON  PLU=ON  L47
L67         134 SEA FILE=MARPAT ABB=ON  PLU=ON  L48
L68           1 SEA FILE=MARPAT ABB=ON  PLU=ON  (L62 OR L63 OR L64 OR L65 OR
              L66 OR L67) AND L30


=> file wpix
FILE 'WPIX' ENTERED AT 11:23:55 ON 19 JUL 2006
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FILE LAST UPDATED:          14 JUL 2006      <20060714/UP>
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MOST RECENT DERWENT UPDATE:     200645        <200645/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
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http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS
    INDEX ENHANCEMENTS PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<
'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d que nos L78
L14             STR
L35          16 SEA FILE=WPIX SSS FUL L14
L36           2 SEA FILE=WPIX ABB=ON  PLU=ON  L35/DCR
L37           2 SEA FILE=WPIX ABB=ON  PLU=ON  (RAEA00/DCN OR RAEA01/DCN OR
                RAEA02/DCN OR RAEA03/DCN OR RAEA04/DCN OR RAEA05/DCN OR
                RAEA07/DCN OR RAEA08/DCN OR RAE9ZS/DCN OR RAE9ZT/DCN OR
                RAE9ZU/DCN OR RAE9ZV/DCN OR RAE9ZW/DCN OR RAE9ZX/DCN OR
                RAE9ZY/DCN OR RAFSCY/DCN)
L38           2 SEA FILE=WPIX ABB=ON  PLU=ON  (902542-0-0-0/DCRE OR 902543-0-0-
                0/DCRE OR 902544-1-0-0/DCRE OR 902544-2-0-0/DCRE OR 902546-0-0-
                0/DCRE OR 902547-0-0-0/DCRE OR 902548-1-0-0/DCRE OR 902548-2-0-
                0/DCRE OR 902550-1-0-0/DCRE OR 902551-0-0-0/DCRE OR 902552-1-0-
                0/DCRE OR 902552-2-0-0/DCRE OR 902553-0-0-0/DCRE OR 902557-0-0-
                0/DCRE OR 902558-0-0-0/DCRE OR 976436-1-0-0/DCRE)
L39           2 SEA FILE=WPIX ABB=ON  PLU=ON  (L36 OR L37 OR L38)
L43         275 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RAULT S?/AU
L44         256 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LANCELOT J?/AU
L45         212 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KOPP M?/AU
L46         121 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CAIGNARD D?/AU
L47         516 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PFEIFFER B?/AU
L48         511 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RENARD P?/AU
L50          86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L43 AND (L44 OR L45 OR L46 OR
                L47 OR L48)
L51          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L44 AND (L45 OR L46 OR L47 OR
                L48)
L52           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45 AND (L46 OR L47 OR L48)
L53          91 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L46 AND (L47 OR L48)
L54         128 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L47 AND L48
L56          21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L50 AND (L51 OR L52 OR L53 OR
                L54)
L57          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND (L52 OR L53 OR L54)
L58           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L52 AND (L53 OR L54)
L77          10 SEA FILE=WPIX ABB=ON  PLU=ON  (L56 OR L57 OR L58)
L78           1 SEA FILE=WPIX ABB=ON  PLU=ON  L77 AND L39


=> d que nos L77
L43         275 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RAULT S?/AU
L44         256 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LANCELOT J?/AU
L45         212 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KOPP M?/AU
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L46          121 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CAIGNARD D?/AU
L47          516 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PFEIFFER B?/AU
L48          511 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RENARD P?/AU
L50           86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L43 AND (L44 OR L45 OR L46 OR
                 L47 OR L48)
L51           14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L44 AND (L45 OR L46 OR L47 OR
                 L48)
L52            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45 AND (L46 OR L47 OR L48)
L53           91 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L46 AND (L47 OR L48)
L54          128 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L47 AND L48
L56           21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L50 AND (L51 OR L52 OR L53 OR
                 L54)
L57           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND (L52 OR L53 OR L54)
L58            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L52 AND (L53 OR L54)
L77           10 SEA FILE=WPIX ABB=ON  PLU=ON  (L56 OR L57 OR L58)


=> d que nos L75
L14              STR
L35           16 SEA FILE=WPIX SSS FUL L14
L36            2 SEA FILE=WPIX ABB=ON  PLU=ON  L35/DCR
L37            2 SEA FILE=WPIX ABB=ON  PLU=ON  (RAEA00/DCN OR RAEA01/DCN OR
                 RAEA02/DCN OR RAEA03/DCN OR RAEA04/DCN OR RAEA05/DCN OR
                 RAEA07/DCN OR RAEA08/DCN OR RAE9ZS/DCN OR RAE9ZT/DCN OR
                 RAE9ZU/DCN OR RAE9ZV/DCN OR RAE9ZW/DCN OR RAE9ZX/DCN OR
                 RAE9ZY/DCN OR RAFSCY/DCN)
L38            2 SEA FILE=WPIX ABB=ON  PLU=ON  (902542-0-0-0/DCRE OR 902543-0-0-
                 0/DCRE OR 902544-1-0-0/DCRE OR 902544-2-0-0/DCRE OR 902546-0-0-
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                 0/DCRE OR 902550-1-0-0/DCRE OR 902551-0-0-0/DCRE OR 902552-1-0-
                 0/DCRE OR 902552-2-0-0/DCRE OR 902553-0-0-0/DCRE OR 902557-0-0-
                 0/DCRE OR 902558-0-0-0/DCRE OR 976436-1-0-0/DCRE)
L39            2 SEA FILE=WPIX ABB=ON  PLU=ON  (L36 OR L37 OR L38)
L69           26 SEA FILE=WPIX ABB=ON  PLU=ON  RAULT S?/AU
L70           22 SEA FILE=WPIX ABB=ON  PLU=ON  LANCELOT J?/AU
L71           54 SEA FILE=WPIX ABB=ON  PLU=ON  KOPP M?/AU
L72           58 SEA FILE=WPIX ABB=ON  PLU=ON  CAIGNARD D?/AU
L73          128 SEA FILE=WPIX ABB=ON  PLU=ON  PFEIFFER B?/AU
L74          239 SEA FILE=WPIX ABB=ON  PLU=ON  RENARD P?/AU
L75            1 SEA FILE=WPIX ABB=ON  PLU=ON  L39 AND (L69 OR L70 OR L71 OR
                 L72 OR L73 OR L74)


=> s L78 or L77 or L75
L80           10 L78 OR L77 OR L75

=> => dup rem L79 L80 L68
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PROCESSING COMPLETED FOR L79
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PROCESSING COMPLETED FOR L80
PROCESSING COMPLETED FOR L68
L81 23 DUP REM L79 L80 L68 (9 DUPLICATES REMOVED)
ANSWERS '1-21' FROM FILE HCAPLUS
ANSWERS '22-23' FROM FILE WPIX

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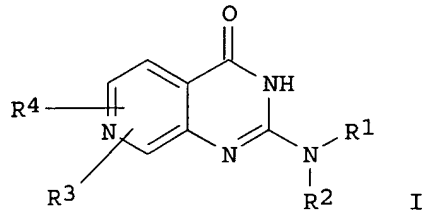
this case

L81 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:370797 HCAPLUS
DOCUMENT NUMBER: 140:375180
TITLE: Preparation of pyridopyrimidinones as hypolipemic agents
INVENTOR(S): **Rault, Sylvain; Lancelot, Jean Charles; Kopp, Marina; Caignard, Daniel Henri; Pfeiffer, Bruno; Renard, Pierre**
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Fr. Demande, 22 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2846657	A1	20040507	FR 2002-13804	20021105
FR 2846657	B1	20041224		
CA 2503995	AA	20040527	CA 2003-2503995	20031104
WO 2004043956	A1	20040527	WO 2003-FR3274	20031104
WO 2004043956	C1	20050609		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003292320	A1	20040603	AU 2003-292320	20031104
EP 1560826	A1	20050810	EP 2003-767886	20031104
EP 1560826	B1	20060412		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015801	A	20050920	BR 2003-15801	20031104
CN 1711260	A	20051221	CN 2003-80102713	20031104
JP 2006512317	T2	20060413	JP 2004-550726	20031104
AT 323092	E	20060415	AT 2003-767886	20031104
US 2005288311	A1	20051229	US 2005-533697	20050503
NO 2005002683	A	20050603	NO 2005-2683	20050603
PRIORITY APPLN. INFO.:			FR 2002-13804 A	20021105
			WO 2003-FR3274 W	20031104

OTHER SOURCE(S): MARPAT 140:375180
GI



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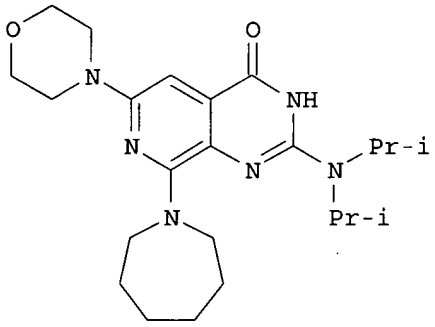


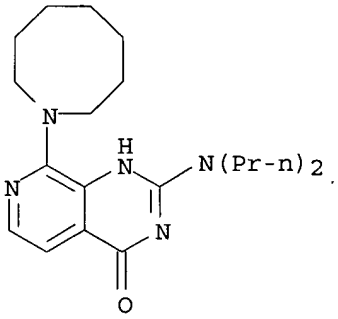
II

AB Title compds. I [wherein R1, R2 = independently H, alkyl, or R1NR2 = heterocycle; R3 = halo, alkoxy, (un)substituted aryl; R4 = H, NH2 and derivs.; their enantiomers, diastereoisomers, tautomers, and their addition salts with a pharmaceutically acceptable acid or base] were prepared as hypolipemic agents. For example, II was prepared by reacting 3-amino-2-azepano-6-(4-morpholinyl)pyridine with ethoxycarbonyl isothiocyanate in the presence of thiourea in DMF, alkylation with DIPA in the presence of HgCl2 (no isolation of intermediate), and cyclization in DMF ar reflux for 2 h. II at 125 mg/kg and metformin at 250 mg/kg reduced triglycerides to the same level in vivo in obese mice using the insulin resistance associated with obesity model. I activated or inhibited certain kinases (no data). Thus, I are useful for treating cancer, diabetes type II, obesity, hyperlipidemia, hypercholesterolemia, cardiovascular complications, arthrosis, and hypertension.

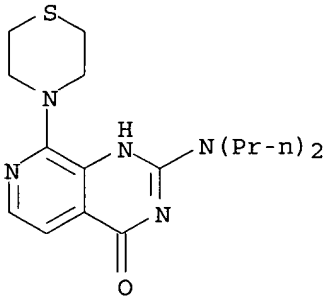
IT **684648-96-2P**, 8-(1-Azocanyl)-2-(dipropylamino)pyrido[3,4-d]pyrimidin-4(3H)-one **684648-98-4P**, 8-(4-Thiomorpholinyl)-2-(dipropylamino)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-00-1P**, 8-[(4aα,8aα)Octahydro-1(2H)-quinolinyl]-2-(dipropylamino)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-02-3P**, 8-[(4aβ,8aα)Octahydro-1(2H)-quinolinyl]-2-(dipropylamino)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-03-4P**, 6,8-Di(1-azepanyl)-2-(dipropylamino)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-05-6P**, 8-(1-Azepanyl)-2-(dipropylamino)-6-(4-morpholinyl)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-07-8P**, 8-(1-Azepanyl)-2,6-di(4-morpholinyl)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-11-4P**, 2-Amino-8-[(3α,5β)-3,5-dimethylmorpholin-4-yl]pyrido[3,4-d]pyrimidin-4(3H)-one **684649-12-5P**, 2-Amino-8-[(3α,5α)-3,5-dimethylmorpholinyl]pyrido[3,4-d]pyrimidin-4(3H)-one **684649-13-6P**, 8-[(3α,5α)-3,5-Dimethylmorpholinyl]-2-(dipropylamino)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-14-7P**, 8-[(3α,5β)-3,5-Dimethylmorpholinyl]-2-(dipropylamino)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-15-8P**,

8-[(3α,5α)-3,5-Dimethylmorpholinyl]-2-(4-morpholinyl)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-16-9P**, 2-Amino-8-(1-azepanyl)-6-(4-morpholinyl)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-17-0P**, 8-Chloro-2-(dipropylamino)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-18-1P**, 2-(Dipropylamino)-8-(1-pyrrolidinyl)pyrido[3,4-d]pyrimidin-4(3H)-one **684649-19-2P**, 8-(3,4-Dimethoxyphenyl)-2-(dipropylamino)pyrido[3,4-d]pyrimidin-4(3H)-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyridopyrimidinones as hypolipemic agents)

RN 684648-96-2 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-(dipropylamino)-8-(hexahydro-1(2H)-azocinyl)- (9CI) (CA INDEX NAME)

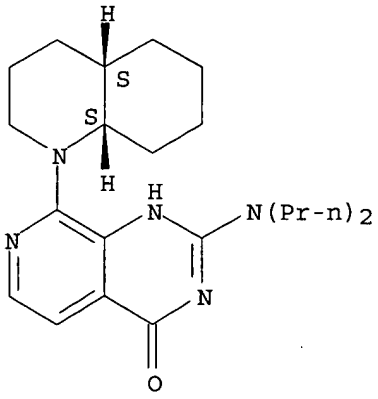


RN 684648-98-4 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-(dipropylamino)-8-(4-thiomorpholinyl)- (9CI) (CA INDEX NAME)



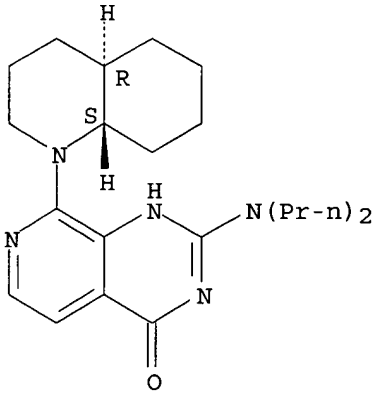
RN 684649-00-1 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-(dipropylamino)-8-[(4aR,8aR)-octahydro-1(2H)-quinolinyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

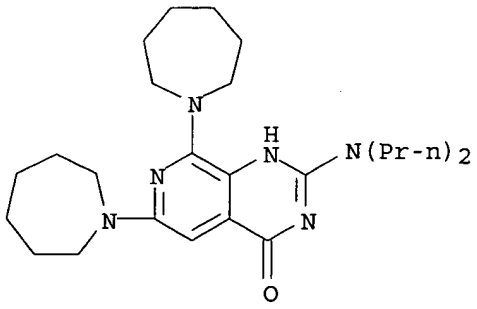


RN 684649-02-3 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-(dipropylamino)-8-[(4aR,8aS)-octahydro-1(2H)-quinolinyl]-, rel- (9CI) (CA INDEX NAME)

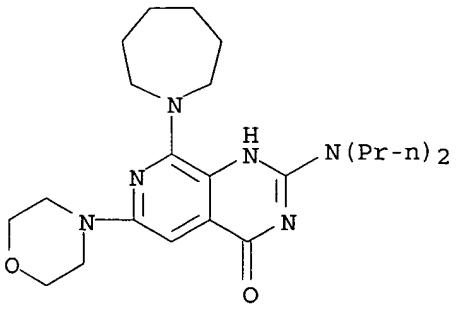
Relative stereochemistry.



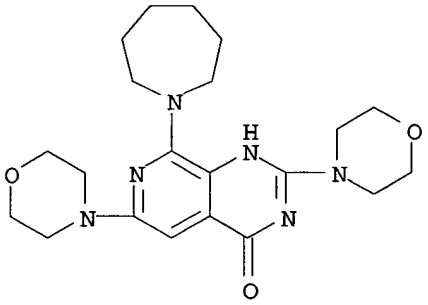
RN 684649-03-4 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-(dipropylamino)-6,8-bis(hexahydro-1H-azepin-1-yl)- (9CI) (CA INDEX NAME)



RN 684649-05-6 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-(dipropylamino)-8-(hexahydro-1H-azepin-1-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

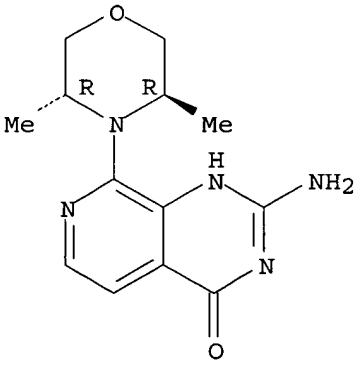


RN 684649-07-8 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 8-(hexahydro-1H-azepin-1-yl)-2,6-di-4-morpholinyl- (9CI) (CA INDEX NAME)



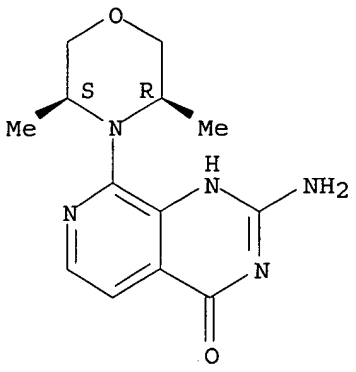
RN 684649-11-4 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-amino-8-[(3R,5R)-3,5-dimethyl-4-morpholinyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



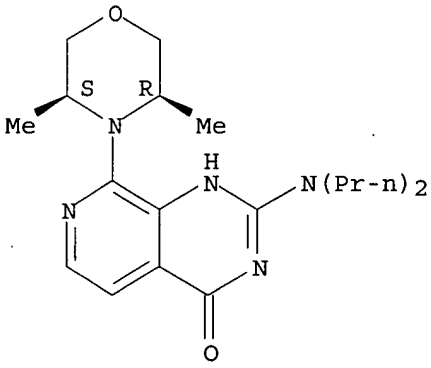
RN 684649-12-5 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-amino-8-[(3R,5S)-3,5-dimethyl-4-morpholinyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



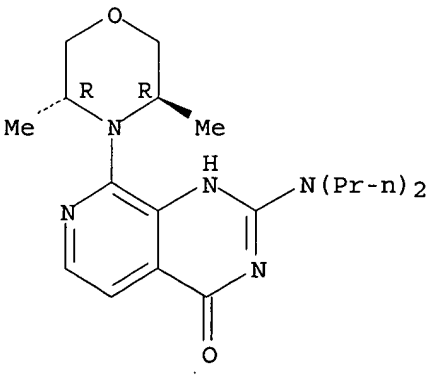
RN 684649-13-6 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 8-[(3R,5S)-3,5-dimethyl-4-morpholinyl]-2-(dipropylamino)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



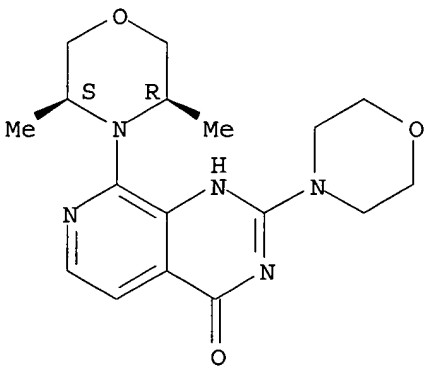
RN 684649-14-7 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 8-[(3R,5R)-3,5-dimethyl-4-morpholinyl]-2-(dipropylamino)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

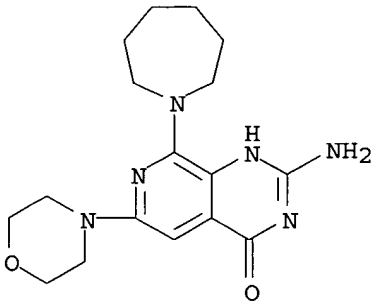


RN 684649-15-8 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 8-[(3R,5S)-3,5-dimethyl-4-morpholinyl]-2-(4-morpholinyl)-, rel- (9CI) (CA INDEX NAME)

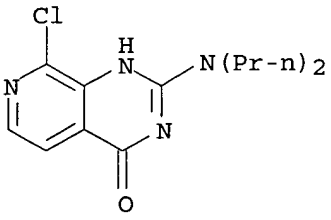
Relative stereochemistry.



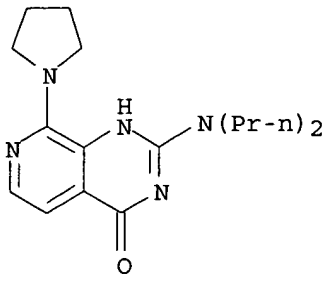
RN 684649-16-9 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-amino-8-(hexahydro-1H-azepin-1-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)



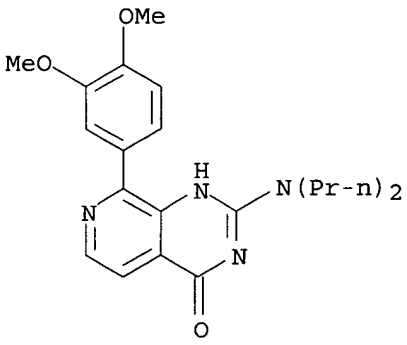
RN 684649-17-0 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 8-chloro-2-(dipropylamino)- (9CI) (CA INDEX NAME)



RN 684649-18-1 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 2-(dipropylamino)-8-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 684649-19-2 HCAPLUS
CN Pyrido[3,4-d]pyrimidin-4(1H)-one, 8-(3,4-dimethoxyphenyl)-2-(dipropylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:370796 HCAPLUS
DOCUMENT NUMBER: 140:375173
TITLE: Preparation of imidazopyridines as AMPK activators for treating diabetes and hyperlipidemia
INVENTOR(S): **Rault, Sylvain; Lancelot, Jean Charles; Kopp, Marina; Caignard, Daniel Henri; Pfeiffer, Bruno; Renard, Pierre**; Bizot Espiard, Jean Guy
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Fr. Demande, 21 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

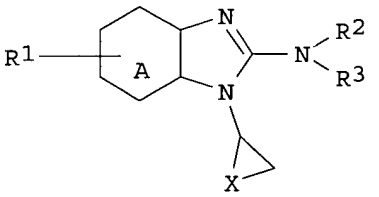
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2846656	A1	20040507	FR 2002-13802	20021105
FR 2846656	B1	20041224		
CA 2504008	AA	20040527	CA 2003-2504008	20031104
WO 2004043957	A1	20040527	WO 2003-FR3277	20031104

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003292323	A1	20040603	AU 2003-292323		20031104
EP 1558612	A1	20050803	EP 2003-767889		20031104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003015800	A	20050920	BR 2003-15800		20031104
CN 1711261	A	20051221	CN 2003-80102714		20031104
JP 2006508111	T2	20060309	JP 2004-550729		20031104
US 2006069117	A1	20060330	US 2005-533699		20050503
NO 2005002710	A	20050606	NO 2005-2710		20050606
PRIORITY APPLN. INFO.:			FR 2002-13802	A	20021105
			WO 2003-FR3277	W	20031104

OTHER SOURCE(S): MARPAT 140:375173
GI



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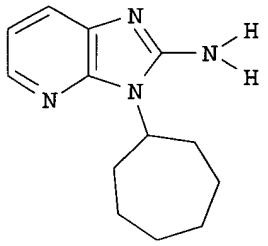


II

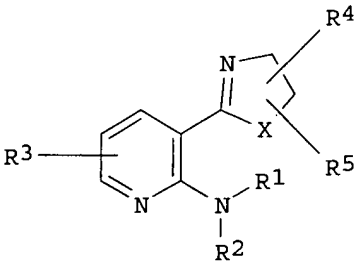
AB Title compds. I [wherein R1 = H, halo, polyhalogeno/alkyl, CN, NO2, hydroxycarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, or dialkylaminocarbonyl; R2 = H, alkyl, (un)substituted hetero/aryl; R3 = H, alkyl; X = (CH2)n; n = 1-6; A = pyridine ring; their enantiomers, diastereoisomers, and their addition salts with a pharmaceutically acceptable acid or base] were prepared as AMP protein kinase (AMPK) activators for treating diabetes and hyperlipidemia. Thus, II (m.p. = 210°) was prepared by reaction of 3-amino-2-cycloheptylaminopyridine with ethoxycarbonyl isothiocyanate in DMF for 3 h, intramol. cyclization in MeOH in the presence of base, and ethoxycarbonyl deprotection in the presence of gaseous HCl and dioxane at reflux for 12 h. II, at 500 μM, activated AMP kinase after 30 min by 312% compared to 178% activation by 5-aminoimidazole-4-carboxamidoriboside in a cellular model. II at 125 mg/kg and metformin at 250 mg/kg reduced triglycerides to the same level in rats. Thus, I are useful for treating hypercholesterolemia, diabetes,

hyperlipidemia, obesity, and cardiovascular complications.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10 L81 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:370795 HCAPLUS
DOCUMENT NUMBER: 140:375078
TITLE: Preparation of pyridines as hypoglycemic agents for treating diabetes and obesity
INVENTOR(S): **Rault, Sylvain**; **Kopp, Marina**; **Lancelot, Jean Charles**; Lemaitre, Stephane; **Pfeiffer, Bruno**; Bizot Espiard, Jean Guy; **Renard, Pierre**
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Fr. Demande, 19 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2846655	A1	20040507	FR 2002-13801	20021105
FR 2846655	B1	20041224		
WO 2004043947	A1	20040527	WO 2003-FR3275	20031104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
AU 2003292321	A1	20040603	AU 2003-292321	20031104
PRIORITY APPLN. INFO.:			FR 2002-13801 A	20021105
			WO 2003-FR3275 W	20031104

OTHER SOURCE(S): MARPAT 140:375078
GI



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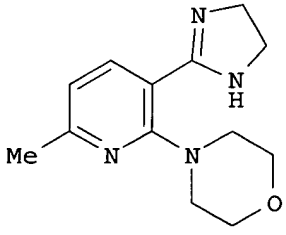


II

AB Title compds. I [wherein R1, R2 = independently H, cyclo/alkyl, (un)substituted hetero/aryl, or R1NR2 = (un)substituted (non)aromatic heterocycle; R3 = H, alkyl, alkoxy, OH, CN, NH2, etc.; R4, R5 = independently H, alkyl; X = O, S, NH and derivs. with certain compds. absent; their enantiomers, diastereomers, tautomers, and their addition salts

with a pharmaceutically acceptable acid or base, with provisos] were prepared as hypoglycemic agents for treating diabetes and obesity. For example, II (m.p. = 147°) was prepared by N-alkylation of morpholine with 2-chloronicotinonitrile, and cyclization of nitrile with 1,2-propanediamine in the presence of P2S5. II reduced glycemia in non-diabetic Wistar rats, STZ-induced diabetes Wistar rats, and Zucker rats by 16/1.4 %, 21/1.93 %, and 9/1.24 %, resp. when administered orally at a dose of 10 mg/kg. II was non-toxic at a maximum concentration of 1024 mg/kg.

Thus, I are useful for treating diabetes and obesity.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2004:370794 HCAPLUS
DOCUMENT NUMBER: 140:375077
TITLE: Preparation of 2,3-dihydro-4(1H)-pyridinones as memory enhancers and analgesics
INVENTOR(S): **Rault, Sylvain**; Leflemme, Nicolas; Dallemagne, Patrick; Lestage, Pierre; Lockhart, Brian; Danober, Laurence; **Pfeiffer, Bruno**; **Renard, Pierre**
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Fr. Demande, 24 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2846654	A1	20040507	FR 2002-13803	20021105
CA 2503993	AA	20040527	CA 2003-2503993	20031104
WO 2004043952	A1	20040527	WO 2003-FR3276	20031104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003292322	A1	20040603	AU 2003-292322	20031104
EP 1560825	A1	20050810	EP 2003-767888	20031104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015996	A	20050927	BR 2003-15996	20031104
CN 1705660	A	20051207	CN 2003-80101823	20031104
JP 2006508110	T2	20060309	JP 2004-550728	20031104
US 2006019995	A1	20060126	US 2005-533784	20050504
NO 2005002598	A	20050530	NO 2005-2598	20050530

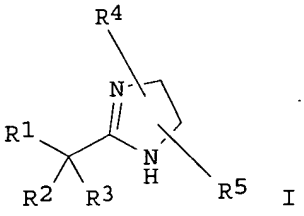
PRIORITY APPLN. INFO.: FR 2002-13803 A 20021105
WO 2003-FR3276 W 20031104

OTHER SOURCE(S): MARPAT 140:375077
GI

FR 2846328	A1	20040430	FR 2002-13194		20021023
FR 2846328	B1	20041210			
JP 2004143167	A2	20040520	JP 2003-357410		20031017
US 2004087638	A1	20040506	US 2003-689394		20031020
US 6875788	B2	20050405			
BR 2003004634	A	20040601	BR 2003-4634		20031021
CA 2445817	AA	20040423	CA 2003-2445817		20031022
AT 288432	E	20050215	AT 2003-292634		20031022
NZ 529084	A	20050429	NZ 2003-529084		20031022
PT 1413579	T	20050531	PT 2003-292634		20031022
ES 2236672	T3	20050716	ES 2003-3292634		20031022
AU 2003257606	A1	20040513	AU 2003-257606		20031023
ZA 2003008265	A	20040709	ZA 2003-8265		20031023
HK 1063320	A1	20060504	HK 2004-106086		20040813
US 2005143440	A1	20050630	US 2005-69094		20050301
PRIORITY APPLN. INFO.:			FR 2002-13194	A	20021023
			US 2003-689394	A3	20031020

OTHER SOURCE(S): MARPAT 140:357344

GI



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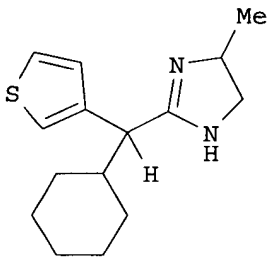


II

AB Title compds. I [wherein R1 = (un)substituted heteroaryl; R2 = (un)substituted cycloalkyl; R3 = H, alkyl; R4, R5 = independently H, halo, polyhalogeno/alkyl, etc.; their enantiomers, diastereomers, tautomers, and their salts of addition with a pharmaceutically acceptable acid or base; with provisos] were prepared as antidiabetic agents. For example, II was prepared by cyclocondensation of cyclohexyl(3-thienyl)acetonitrile (preparation given) with 1,2-propanediamine in the presence of PS5. II was tested for use as a drug for non-insulin dependent diabetes and hyperlipidemia associated with obesity (glycemia reduced 13 - 18% at 10 mg/kg). I are useful for treating diabetes mellitus type II, obesity, diabetes type I, hyperlipidemia, hypercholesterolemia, and cardiovascular complications.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2000:790170 HCAPLUS

DOCUMENT NUMBER: 133:335170

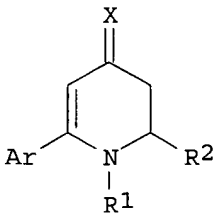
TITLE: Preparation of 1-aza-2-alkyl-6-arylcycloalkanes useful as memory enhancers

INVENTOR(S): **Rault, Sylvain**; Renault, Olivier; Guillon, Jean; Dallemagne, Patrick; **Renard, Pierre**; **Pfeiffer, Bruno**; Lestage, Pierre; Lebrun, Marie-Cecile

PATENT ASSIGNEE(S): Adir et Compagnie, Fr.; Servier Lab.

SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent



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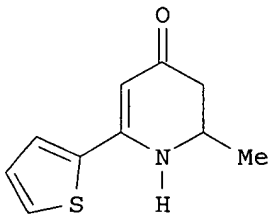
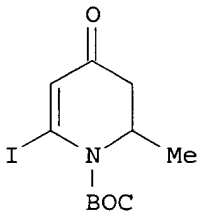


II



III

AB Title compds. I [wherein R1 = H, aryl/alkyl, acyl, alkoxycarbonyl, arylalkoxycarbonyl, CF3; R2 = H, alkyl; X = O or NOR3; R3 = H, (un)substituted alkyl; Ar = hetero/aryl; their enantiomers, diastereomers isomers, and their addition salts with a pharmaceutically acceptable acid] were prepared as memory enhancers and analgesics. For example, II was prepared by Pd-cross coupling of iodide III with 2-thienylboronic acid, and Boc deprotection. II inhibited abdominal cramps induced by PBQ in mice by 48% when administered i.p..

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2004:348013 HCAPLUS
DOCUMENT NUMBER: 140:357344
TITLE: Preparation of imidazolines as hypoglycemic agents
INVENTOR(S): **Rault, Sylvain**; **Kopp, Marina**; **Lancelot, Jean-Charles**; Lemaitre, Stephane; **Caignard, Daniel-Henri**; Bizot-espiard, Jean-Guy; **Renard, Pierre**
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1413579	A1	20040428	EP 2003-292634	20031022
EP 1413579	B1	20050202		

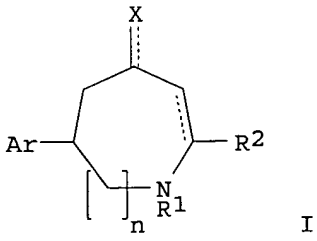
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1050530	A1	20001108	EP 2000-401199	20000502
EP 1050530	B1	20031022		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
FR 2793246	A1	20001110	FR 1999-5600	19990503
FR 2793246	B1	20010629		
JP 2000351766	A2	20001219	JP 2000-127382	20000427
JP 3224376	B2	20000427		
CN 1277194	A	20001220	CN 2000-118158	20000430
CN 1145612	B	20040414		
NO 2000002315	A	20001106	NO 2000-2315	20000502
NO 315850	B1	20031103		
NZ 504299	A	20010126	NZ 2000-504299	20000502
US 6323222	B1	20011127	US 2000-561646	20000502
AT 252558	E	20031115	AT 2000-401199	20000502
PT 1050530	T	20040227	PT 2000-401199	20000502
ES 2209777	T3	20040701	ES 2000-401199	20000502
CA 2308783	AA	20001103	CA 2000-2308783	20000503
CA 2308783	C	20041019		
ZA 2000002151	A	20001107	ZA 2000-2151	20000503
BR 2000002076	A	20010123	BR 2000-2076	20000503
AU 763685	B2	20030731	AU 2000-31324	20000503
HK 1032235	A1	20040930	HK 2001-102865	20010423
US 2002042413	A1	20020411	US 2001-964085	20010926
US 6451789	B2	20020917		

PRIORITY APPLN. INFO.: FR 1999-5600 A 19990503
US 2000-561646 A3 20000502

OTHER SOURCE(S): MARPAT 133:335170
GI



I

AB The title compds. I [n = 0, 1; R1 = H, arylalkyl, alkyl, acyl, etc.; R2 = alkyl; X = O, Cl, OR3, SR4, NOR5; Ar = aryl, heteroaryl], memory enhancers, were prepared E.g., 2-(3-chlorophenyl)-6-methyl-2,3-dihydro-4(1H)-pyridinone was prepared
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1996:485727 HCAPLUS
DOCUMENT NUMBER: 125:142700
TITLE: Tricyclic oxime ethers process for their preparation

and pharmaceutical compositions containing them

INVENTOR(S): **Rault, Sylvain**; Robba, Max; **Lancelot, Jean-Charles**; Prunier, Herve; **Renard, Pierre**; **Pfeiffer, Bruno**; Guardiola-Lemaitre, Beatrice; Rettori, Marie-Claire

PATENT ASSIGNEE(S): Adir Et Compagnie, Fr.

SOURCE: Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 718299	A1	19960626	EP 1995-402865	19951219
EP 718299	B1	20000405		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
FR 2728571	A1	19960628	FR 1994-15431	19941222
FR 2728571	B1	19970131		
CA 2165618	AA	19960623	CA 1995-2165618	19951219
CA 2165618	C	20010410		
AT 191483	E	20000415	AT 1995-402865	19951219
PT 718299	T	20000731	PT 1995-402865	19951219
ES 2147271	T3	20000901	ES 1995-402865	19951219
FI 9506136	A	19960623	FI 1995-6136	19951220
AU 9540593	A1	19960627	AU 1995-40593	19951220
AU 693615	B2	19980702		
NO 9505215	A	19960624	NO 1995-5215	19951221
ZA 9510901	A	19960624	ZA 1995-10901	19951221
JP 08231554	A2	19960910	JP 1995-333347	19951221
JP 2937837	B2	19990823		
US 5627203	A	19970506	US 1995-576678	19951221
CN 1131155	A	19960918	CN 1995-120144	19951222
CN 1066449	B	20010530		
CN 1261073	A	20000726	CN 1999-120993	19991203
GR 3033507	T3	20000929	GR 2000-401198	20000525

PRIORITY APPLN. INFO.: FR 1994-15431 A 19941222

OTHER SOURCE(S): MARPAT 125:142700

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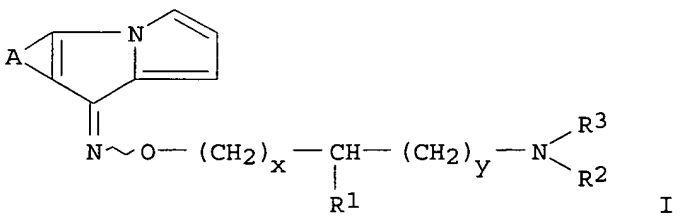

I

AB The present invention concerns compds. I, in which A represents a thieno group, x and y are independently 0-4, R1 is H, alkyl, alkenyl, cycloalkyl, OH, alkoxy, substituted Ph, phenylalkyl, substituted phenoxy, R2 and R3 are H, alkyl, alkenyl, cycloalkyl, substituted indanyl, substituted Ph, phenylalkyl, or R2 and R3 form azacycloalkyl rings, and their oxalates or fumarates. I, e.g. II (X = NOCHPhCH2CH2NMe2) are prepared from the ketone, e.g II (X = O), via hydroxyimination followed by O-alkylation, e.g with

PhCHClCH2CH2NMe2·HCl. I were tested as serotoninergic receptor antagonists (IC50 1.1 x 10 -10 to 10-4 M), anxiolytics and antidepressants.

L81 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1994:217734 HCAPLUS
DOCUMENT NUMBER: 120:217734
TITLE: Pyrrolothienopyrazine serotonin 5-HT3 receptor antagonists
INVENTOR(S): **Rault, Sylvain**; **Lancelot, Jean Charles**; Pilo Vincente, Juan Carlos; Robba, Max; Guardiola-Lemaitre, Beatrice; **Renard, Pierre**; Adam, Gerard
PATENT ASSIGNEE(S): ADIR et Compagnie, Fr.
SOURCE: Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 573360	A1	19931208	EP 1993-401416	19930603
EP 573360	B1	19980826		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
FR 2691967	A1	19931210	FR 1992-6800	19920605
FR 2691967	B1	19950609		
AT 170187	E	19980915	AT 1993-401416	19930603
ES 2123038	T3	19990101	ES 1993-401416	19930603
CA 2097779	AA	19931206	CA 1993-2097779	19930604
AU 9340059	A1	19931209	AU 1993-40059	19930604
AU 659738	B2	19950525		
ZA 9303942	A	19931230	ZA 1993-3942	19930604
JP 06172363	A2	19940621	JP 1993-134922	19930604
JP 07094460	B4	19951011		
PRIORITY APPLN. INFO.:			FR 1992-6800 A	19920605
OTHER SOURCE(S):	MARPAT 120:217734			

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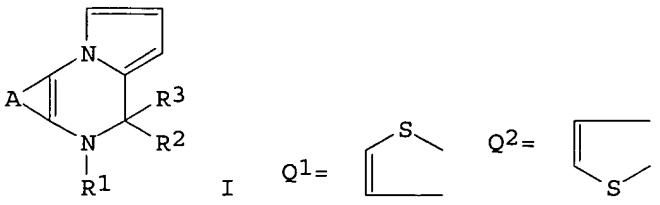

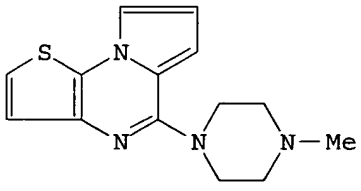

II

AB The title compds. I [A = (un)substituted Q1, (un)substituted Q2; R1R2 form

a double bond and R3 represents a Cl atom, a substituted amine or heterocyclyl group, or no group or R1 may represent a H and R2R3 a :O], which are highly specific serotonin 5-HT3 receptor antagonists (no data), useful in the treatment of depression (no data), stress (no data) psychoses (no data), migraine headache (no data), etc., are prepared and I-containing formulations presented. Thus, 2-(pyrrol-1-yl)-3-thenoyl nitride was refluxed in 1,2-dichlorobenzene, the intermediate heated in the presence of POCl2, and condensed with 1-methylpiperazine, producing pyrazine II, m.p. 82°.

L81 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:115127 HCAPLUS
DOCUMENT NUMBER: 140:321259
TITLE: Design, synthesis, and evaluation of novel thienopyrrolizinones as antitubulin agents
AUTHOR(S): Lisowski, Vincent; Leonce, Stephane; Kraus-Berthier, Laurence; Santos, Jana Sopkova-de Oliveira; Pierre, Alain; Atassi, Ghanem; **Caignard, Daniel-Henri ; Renard, Pierre; Rault, Sylvain**
CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie UFR des Sciences Pharmaceutiques, Universite de Caen, Caen, 14032, Fr.
SOURCE: Journal of Medicinal Chemistry (2004), 47(6), 1448-1464
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:321259
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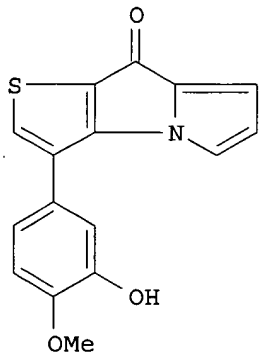

I

AB The structure-activity relationship study of a new 3-aryl-8-H-thieno[2,3-b]pyrrolizin-8-one series of antitubulin agents was described. The pharmacol. results from the National Cancer Institute in vitro human disease oriented tumor cell line screening allowed the identification of 3-(4-methoxyphenyl)-8H-thieno[2,3-b]pyrrolizin-8-one (NSC 676693) as a very efficient antitumor drug in all cancer cell lines tested. This required a definition of structural requirements essential for this antiproliferative activity. Among all analogs synthesized in this study, 3-(3-hydroxy-4-methoxyphenyl)-8H-thieno[2,3-b]pyrrolizin-8-one (I) was the most promising, being 10-fold more potent than NSC 676693. Its activity over a panel of nine tumoral cell lines was in the nanomolar range for all of the histol. types tested, and surprisingly, the resistant KB-A1 cell

line was also sensitive to this compound Moreover, a flow cytometric study showed that L1210 cells treated by the most potent compds. were arrested in the G2/M phases of the cell cycle with a significant percentage of cells having reinitiated a cycle of DNA synthesis without cell division. This interesting pharmacol. profile, resulting from inhibition of tubulin polymerization, encouraged us to perform preliminary in vivo studies that led to a new prodrug chemical approach.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:928395 HCAPLUS
DOCUMENT NUMBER: 138:170063
TITLE: New Benzo[h][1,6]naphthyridine and Azepino[3,2-c]quinoline Derivatives as Selective Antagonists of 5-HT4 Receptors: Binding Profile and Pharmacological Characterization
AUTHOR(S): Hinschberger, Antoine; Butt, Sabrina; Lelong, Veronique; Boulouard, Michel; Dumuis, Aline; Dauphin, Francois; Bureau, Ronan; **Pfeiffer, Bruno**; **Renard, Pierre**; **Rault, Sylvain**
CORPORATE SOURCE: ATBI, Universite de Caen, Caen, 14032, Fr.
SOURCE: Journal of Medicinal Chemistry (2003), 46(1), 138-147
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:170063
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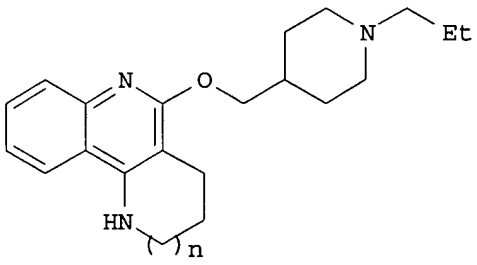

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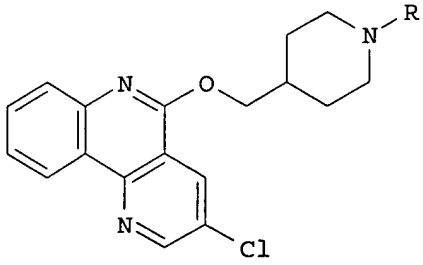

II

AB Benzo[h][1,6]naphthyridinyloxymethylpiperidines such as I (n = 1),

azepino[3,2-c]quinolinyloxymethylpiperidines such as I (n = 2), and benzonaphthyridines II (R = EtCH2, Bu) were prepared as potential 5-HT4 receptor antagonists. Benzonaphthyridinyloxymethylpiperidines and azepinoquinolinyloxymethylpiperidines were prepared by substitution reactions of chlorobenzonaphthyridines and chloroazepinoquinolines with N-substituted 4-piperidinemethanols. The binding of benzonaphthyridinyloxymethylpiperidines and azepinoquinolinyloxymethylpipe ridines to the 5-HT4 receptor decreased markedly when chlorine atom substituents were present on the aromatic ring; N-Pr and N-Bu substituents on the piperidine moiety yield compds. such as I (n = 1) which bound to 5-HT4 receptors with nanomolar affinities. I (n = 1) acted as an antagonist/low partial agonist of the 5-HT4 receptor. I (n = 1) also showed potent analgesic activity in mice at doses of 0.01-1 mg/kg.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:805388 HCAPLUS
DOCUMENT NUMBER: 138:238138
TITLE: A versatile synthesis of 2-amino-4H-pyrido[1,2-a][1,3,5]triazin-4-ones from 2-aminopyridines
AUTHOR(S): **Kopp, Marina**; **Lancelot, Jean-Charles** ; Dagdag, Said; Miel, Hugues; **Rault, Sylvain**
CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie, Universite de Caen-Basse Normandie, Caen, 14032, Fr.
SOURCE: Journal of Heterocyclic Chemistry (2002), 39(5), 1061-1064
CODEN: JHTCAD; ISSN: 0022-152X
PUBLISHER: HeteroCorporation
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:238138
AB The quasi-one pot synthesis of new 2-amino-4H-pyrido[1,2-a]-1,3,5-triazin-4-ones starting from 2-aminopyridine and 2-aminopicolines is herein described in order to obtain a library of cyclic guanidines.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:938490 HCAPLUS
DOCUMENT NUMBER: 139:30285
TITLE: Synthesis of New Aromatic Pyrrolo[2,1-c][1,4]benzodiazepines and Pyrrolo[1,2-a]thieno[3,2-e][1,4]diazepines as Anti-tumoral Agents
AUTHOR(S): Lisowski, Vincent; Fabis, Frederic; Pierre, Alain; **Caignard, Daniel-Henri**; **Renard, Pierre** ; **Rault, Sylvain**
CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie-UFR des Sciences Pharmaceutiques 5, Caen, 14032, Fr.
SOURCE: Journal of Enzyme Inhibition and Medicinal Chemistry (2002), 17(6), 403-407
CODEN: JEIMAZ; ISSN: 1475-6366
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:30285
AB Diazepine analogs of thieno[2,3-b]pyrrolizin-8-ones were synthesized by aromatization of 2-hydroxypyrrolo[1,2-a]thieno[3,2-e][1,4]diazepines.

These compds. were evaluated in vitro for their antiproliferative activity against the L1210 leukemia cell line. The activity of these compds. was in the micromolar range, the best result being for the mixture of the isomers which showed a 0.35 μM IC50 against cell growth.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:612043 HCAPLUS
DOCUMENT NUMBER: 135:371658
TITLE: Design, synthesis and antiproliferative activity of tripentones: A new series of antitubulin agents
AUTHOR(S): Lisowski, V.; Enguehard, C.; **Lancelot, J.-C.**; **Caignard, D.-H.**; Lambel, S.; Leonce, S.; Pierre, A.; Atassi, G.; **Renard, P.**; **Rault, S.**
CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie, UFR des Sciences Pharmaceutiques, Caen, 14032, Fr.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(16), 2205-2208
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:371658
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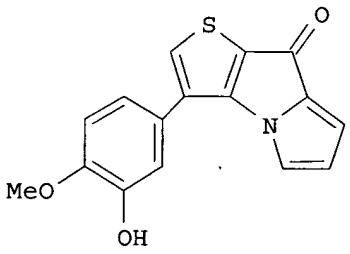

I

AB Structure-activity relationship studies of a new series of tripentones (thieno[2,3-b]pyrrolizin-8-ones), led to the prepare of several derivs. with antiproliferative activities. The most promising 3-(3-hydroxy-4-methoxyphenyl)thieno[2,3-b]pyrrolizin-8-one (I) (leukemia L1210, IC50=15 nM) was shown to be a potent inhibitor of tubulin polymerization

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:779581 HCAPLUS
DOCUMENT NUMBER: 136:183790
TITLE: Synthesis of novel pyrazolopyrrolopyrazines, potential analogs of sildenafil
AUTHOR(S): **Kopp, Marina**; **Lancelot, Jean-Charles**; Dallemagne, Patrick; **Rault, Sylvain**
CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie, Caen, 14032, Fr.
SOURCE: Journal of Heterocyclic Chemistry (2001), 38(5), 1045-1050

CODEN: JHTCAD; ISSN: 0022-152X
PUBLISHER: HeteroCorporation
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:183790
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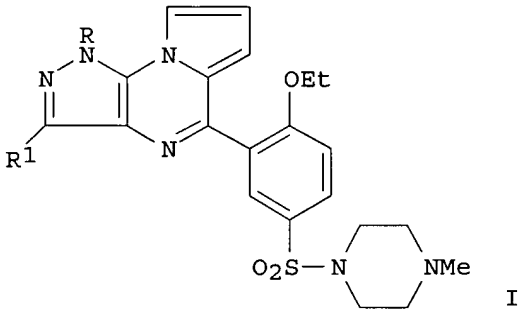

I

AB The pyrazolopyrrolopyrazines I [R = Me, Ph, 4-MeOC6H4, R1 = H; R = Me, R1 = Pr] were prepared as analogs of sildenafil. I were 10-fold less active than sildenafil as PDE-5 inhibitors.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:177391 HCAPLUS
DOCUMENT NUMBER: 135:28643
TITLE: First tricyclic oximino derivatives as 5-HT3 ligands
AUTHOR(S): Baglin, I.; Daveu, C.; **Lancelot, J. C.**; Bureau, R.; Dauphin, F.; **Pfeiffer, B.**; **Renard, P.**; Delagrange, P.; **Rault, S.**
CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie, Universite de Caen, Caen, 14032, Fr.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(4), 453-457
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The design and synthesis of a new type of 5-HT3 ligand with subnanomolar affinity are described. The O-dialkylaminoethyloximinothienopyrrolizine structure was deduced from mol. modeling studies by replacement of an amidine moiety by an oximino one.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:106891 HCAPLUS
DOCUMENT NUMBER: 132:151677
TITLE: Preparation of 8H-thieno-[2,3-b]pyrrolizin-8-ones as anticancer agents
INVENTOR(S): **Rault, Sylvain**; Enguehard, Cucile; **Lancelot, Jean-Charles**; Robba, Max; Atassi, Ghanem; Pierre, Alain; **Caignard, Daniel-Henri**; **Renard, Pierre**
PATENT ASSIGNEE(S): Adir Et Compagnie, Fr.

SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000044572	A2	20000215	JP 1999-210412	19990726
FR 2781482	A1	20000128	FR 1998-9552	19980727
FR 2781482	B1	20010831		
NO 9903608	A	20000128	NO 1999-3608	19990723
NO 313521	B1	20021014		
EP 982308	A1	20000301	EP 1999-401892	19990726
EP 982308	B1	20030226		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9902841	A	20000509	BR 1999-2841	19990726
US 6071945	A	20000606	US 1999-361064	19990726
NZ 336913	A	20000623	NZ 1999-336913	19990726
AT 233266	E	20030315	AT 1999-401892	19990726
CA 2279099	C	20030617	CA 1999-2279099	19990726
CA 2279099	AA	20000127		
ES 2192827	T3	20031016	ES 1999-401892	19990726
ZA 9904817	A	20000202	ZA 1999-4817	19990727
CN 1244529	A	20000216	CN 1999-110693	19990727
CN 1122669	B	20031001		
AU 9941171	A1	20000217	AU 1999-41171	19990727
AU 752505	B2	20020919		
HK 1024244	A1	20040514	HK 2000-103590	20000615

PRIORITY APPLN. INFO.: FR 1998-9552 A 19980727
OTHER SOURCE(S): CASREACT 132:151677; MARPAT 132:151677
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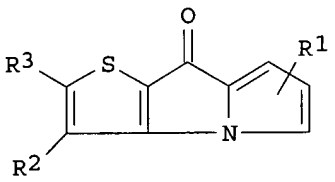

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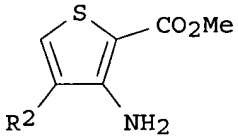

II

AB Title compds. I (R1, R3 = H, halo, C1-6 alkyl, NO2, OH, C1-6 alkoxy, etc.; R2 = (un)substituted aryl, heteroaryl), their isomers, or pharmaceutically acceptable salts are prepared from II (prepared by successive reaction of R2CH2CN (R2 = same as I) with HCO2Et, PhSO2Cl, and methylthio glycolate) via several steps. 4-(2-Methoxyphenyl)-3-(1H-1-pyrrolyl)-2-thiophene-N-pyrrolidinocarboxamide was cyclized in the presence of POCl3 under reflux for 3 h to give 3-(2-methoxyphenyl)-8H-thieno[2,3-b]pyrrolizin-8-one showing in vivo antitumor activity against leukemic P 388.

L81 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:614430 HCAPLUS
DOCUMENT NUMBER: 131:307037
TITLE: Effects of S-21007, a potent 5-HT3 partial agonist, in mouse anxiety

AUTHOR(S): Delagrange, Philippe; Misslin, Rene; Seale, Thomas W.; **Pfeiffer, Bruno**; **Rault, Sylvain**; **Renard, Pierre**
CORPORATE SOURCE: Institut de Recherches Internationales Servier, Courbevoie, 92415, Fr.
SOURCE: Zhongguo Yaoli Xuebao (1999), 20(9), 805-812
CODEN: CYLPDN; ISSN: 0253-9756
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AIM: To study the effect of S-21007, a 5-HT3 partial agonist in different animal models of anxiety in mice. METHODS: S-21007 effects were evaluated in behavior tests after i.p. and oral acute treatment or in the light/dark test after both acute and chronic treatments. RESULTS: S-21007 presented anxiolytic-like properties after acute administration in the light/dark box test, the mirrored chamber test, and the elevated plus-maze at low doses 10 ng·kg-1-100 μg·kg-1, 1-100 μg·kg-1 and 10-100 μg·kg-1, resp. In the light/dark box test, S-21007 was active orally after acute treatment at 100 ng·kg-1-10 mg·kg-1 and after chronic treatment (14 d) at 1-10 μg·kg-1. S-21007 was devoid of sedative or stimulatory effects. CONCLUSION: S-21007 exhibited anxiolytic-like properties. The mechanism of action may be a desensitization of 5-HT3 receptor or an antagonist activity on the 5-HT3 receptors.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:366507 HCAPLUS
DOCUMENT NUMBER: 129:122642
TITLE: Synthesis of new pyrrolo[1,2-a]quinoxalines: potential non-peptide glucagon receptor antagonists
AUTHOR(S): Guillon, Jean; Dallemagne, Patrick; **Pfeiffer, Bruno**; **Renard, Pierre**; Manechez, Dominique; Kervran, Alain; **Rault, Sylvain**
CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie, Lab. de Pharmacochimie, UFR des Sciences Pharmaceutiques, Caen, 14032, Fr.
SOURCE: European Journal of Medicinal Chemistry (1998), 33(4), 293-308
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Synthesis of new pyrrolo[1,2-a]quinoxaline derivs. was achieved starting from various nitroanilines or o-phenylenediamines. Theyshowed little affinity towards glucagon receptors.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:320915 HCAPLUS
DOCUMENT NUMBER: 127:271
TITLE: Novel and Selective Partial Agonists of 5-HT3 Receptors. 2. Synthesis and Biological Evaluation of Piperazinopyridopyrrolopyrazines, Piperazinopyrroloquinoxalines, and Piperazinopyridopyrroloquinoxalines
AUTHOR(S): Prunier, Herve; **Rault, Sylvain**; **Lancelot, Jean-Charles**; Robba, Max;

Renard, Pierre; Delagrange, Philippe; **Pfeiffer, Bruno**; **Caignard, Daniel-Henri**; Misslin, Rene; Guardiola-Lemaitre, Beatrice; Hamon, Michel

CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie, Universite de Caen, Caen, 14032, Fr.

SOURCE: Journal of Medicinal Chemistry (1997), 40(12), 1808-1819
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In continuation of our previous work on piperazinopyrrolothienopyrazine derivs., three series of piperazinopyridopyrrolopyrazines, piperazinopyrroloquinoxalines, and piperazinopyridopyrroloquinoxalines were prepared and evaluated as 5-HT3 receptor ligands. The chemical modifications performed within these new series led to structure-activity relationships regarding both high affinity and selectivity for the 5-HT3 receptors that are in agreement with those established previously for the pyrrolothienopyrazine series. The best compound (8a) obtained in these new series is in the picomolar range of affinity for 5-HT3 receptors with a selectivity higher than 106. Four of the high-affinity 5-HT3 ligands (8a, 15a,b, and 16d) were selected in both the pyridopyrrolopyrazine and the pyrroloquinoxaline series and were characterized in vitro and in vivo as agonists or partial agonists. Compound 8a was also evaluated in the light/dark test where it showed potential anxiolytic-like activity at very low doses per os.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L81 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:241880 HCAPLUS
DOCUMENT NUMBER: 124:289475

TITLE: Novel Selective and Partial Agonists of 5-HT3 Receptors. Part 1. Synthesis and Biological Evaluation of Piperazinopyrrolothienopyrazines

AUTHOR(S): **Rault, Sylvain**; **Lancelot, Jean-Charles**; Prunier, Herve; Robba, Max; **Renard, Pierre**; Delagrange, Philippe; **Pfeiffer, Bruno**; **Caignard, Daniel-Henri**; Guardiola-Lemaitre, Beatrice; Hamon, Michel

CORPORATE SOURCE: Centre d'Etudes et de Recherche sur le Medicament de Normandie, Universite de Caen, Caen, 14032, Fr.

SOURCE: Journal of Medicinal Chemistry (1996), 39(10), 2068-80
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of (piperazinyl)pyrrolo[1,2-a]thieno[3,2-e]pyrazines and (piperazinyl)pyrrolo[1,2-a]thieno[2,3-e]pyrazines was prepared and evaluated in order to determine the necessary requirements for high affinity on the 5-HT3 receptors and high selectivity vs. other 5-HT receptor subtypes. Various substitutions on the piperazine and the thiophene ring of the pyrrolothienopyrazine moieties were systematically explored as well as replacement of the piperazine by other cyclic amines. An example compound is 5-[4-[(4-fluorophenyl)methyl]-1-piperazinyl]pyrrolo[1,2-a]thieno[3,2-e]pyrazine trihydrochloride. These high-affinity compds. have in common a benzyl- or allylpiperazine substituent with no substitutions on the thiophene ring. Five of these compds. were evaluated on the Von

Bezold-Jarisch reflex and were characterized as partial agonists. One of them, 5-[4-(phenylmethyl)-1-piperazinyl]pyrrolo[1,2-a]thieno[3,2-e]pyrazine (fumarate) was shown in vivo at very low dose a potent anxiolytic-like activity in the light/dark test.

L81 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:726818 HCAPLUS
DOCUMENT NUMBER: 126:69969
TITLE: Interaction of S 21007 with 5-HT3 receptors. In vitro and in vivo characterization
AUTHOR(S): Delagrange, Philippe; Emerit, M. Boris; Merahi, Nacera; Abraham, Christine; Morain, Philippe; **Rault, Sylvain**; **Renard, Pierre**; **Pfeiffer, Bruno**; Guardiola-Lemaitre, Beatrice; et al.
CORPORATE SOURCE: IRIS, 6 Place des Pleiades, Courbevoie, 92415, Fr.
SOURCE: European Journal of Pharmacology (1996), 316(2/3), 195-203
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interaction of S 21007 [5-(4-benzyl piperazin-1-yl)4H pyrrolo[1,2-a]thieno[3,2-e]pyrazine] with serotonin 5-HT3 receptors was investigated using biochem., electrophysiol. and functional assays. Binding studies using membranes from N1E-115 neuroblastoma cells showed that S 21007 is a selective high affinity (IC50 = 2.8 nM) 5-HT3 receptor ligand. As expected of an agonist, S 21007 stimulated the uptake of [14C]guanidinium (EC50.apprx.10 nM) in NG 108-15 cells exposed to substance P, and this effect could be prevented by the potent 5-HT3 receptor antagonist ondansetron. In addition, like 5-HT and other 5-HT3 receptor agonists (phenylbiguanide and 3-chloro-phenylbiguanide), S 21007 (EC50 = 27 μM) produced a rapid inward current in N1E-115 cells. The 5-HT3 receptor agonist action of S 21007 was also demonstrated in urethane-anesthetized rats as this drug (120 μg/kg i.v.) triggered the Bezold-Jarisch reflex (rapid fall in heart rate), and this action could be prevented by pretreatment with the potent 5-HT3 receptor antagonist zacopride. Finally, in line with its 5-HT3 receptor agonist properties, S 21007 also triggered emesis in the ferret. Evidence for 5-HT3 receptor antagonist-like properties of S 21007 was also obtained in some of these expts. since previous exposure to this compound prevented both the 5-HT-induced current in N1E-115 cells and the Bezold-Jarisch reflex elicited by an i.v. bolus of 5-HT (30 μg/kg) in urethane-anesthetized rats. These data suggest that S 21007 is a selective 5-HT3 receptor agonist which can exhibit antagonist-like properties either by triggering a long lasting receptor desensitization or by a partial agonist activity at 5-HT3 receptors in some tissues.

L81 ANSWER 22 OF 23 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-149624 [14] WPIX
DOC. NO. CPI: C2000-047071
TITLE: New 8H-thieno(2,3-b)pyrrolizin-8-one derivatives useful as anticancer agents, especially for treating solid tumors.
DERWENT CLASS: B02
INVENTOR(S): ATASSI, G; **CAIGNARD, D H**; ENGUEHARD, C; **LANCELOT, J**; PIERRE, A; **RAULT, S**; **RENARD, P**; ROBBA, M; **CAIGNARD, D**; ROBRA, M; EGUHAD, C; LANSLOT, J C; LART, S; **LANCELOT, J C**

PATENT ASSIGNEE(S): (SERV-N) LES LAB SERVIER; (ADIR) ADIR & CIE
COUNTRY COUNT: 35
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2781482	A1	20000128	(200014)*		22
EP 982308	A1	20000301	(200016)	FR	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
NO 9903608	A	20000128	(200016)		
AU 9941171	A	20000217	(200019)		
JP 2000044572	A	20000215	(200019)		12
CN 1244529	A	20000216	(200027)		
ZA 9904817	A	20000426	(200027)		27
CA 2279099	A1	20000127	(200028)	FR	
HU 9902546	A2	20000428	(200030)		
BR 9902841	A	20000509	(200033)		
US 6071945	A	20000606	(200033)		
NZ 336913	A	20000623	(200038)		
AU 752505	B	20020919	(200272)		
NO 313521	B1	20021014	(200275)		
EP 982308	B1	20030226	(200316)	FR	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 69905524	E	20030403	(200330)		
CA 2279099	C	20030617	(200347)	FR	
ES 2192827	T3	20031016	(200377)		
CN 1122669	C	20031001	(200553)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
FR 2781482	A1	FR 1998-9552	19980727
EP 982308	A1	EP 1999-401892	19990726
NO 9903608	A	NO 1999-3608	19990723
AU 9941171	A	AU 1999-41171	19990727
JP 2000044572	A	JP 1999-210412	19990726
CN 1244529	A	CN 1999-110693	19990727
ZA 9904817	A	ZA 1999-4817	19990727
CA 2279099	A1	CA 1999-2279099	19990726
HU 9902546	A2	HU 1999-2546	19990727
BR 9902841	A	BR 1999-2841	19990726
US 6071945	A	US 1999-361064	19990726
NZ 336913	A	NZ 1999-336913	19990726
AU 752505	B	AU 1999-41171	19990727
NO 313521	B1	NO 1999-3608	19990723
EP 982308	B1	EP 1999-401892	19990726
DE 69905524	E	DE 1999-605524	19990726
		EP 1999-401892	19990726
CA 2279099	C	CA 1999-2279099	19990726
ES 2192827	T3	EP 1999-401892	19990726
CN 1122669	C	CN 1999-110693	19990727

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 752505	B	Previous Publ.	AU 9941171
NO 313521	B1	Previous Publ.	NO 9903608

DE 69905524 E Based on EP 982308
ES 2192827 T3 Based on EP 982308

PRIORITY APPLN. INFO: FR 1998-9552 19980727
AN 2000-149624 [14] WPIX
AB FR 2781482 A UPAB: 20000320
NOVELTY - 8H-Thieno(2,3-b)pyrrolizin-8-one derivatives (I) are new.
DETAILED DESCRIPTION - 8H-Thieno(2,3-b)pyrrolizin-8-one derivatives (I) and salts are new.
R1, R3 = H, halo, 1-6C alkyl, NO2, OH, 1-6C alkoxy, 1-6C trihaloalkyl, 1-6C trihaloalkoxy, NH2, 1-6C alkylamino or di(1-6C alkyl)amino;
R2 = aryl or heteroaryl (both optionally substituted); and
provided that R2 is phenyl optionally p-substituted by Br, Cl, F, OMe or OH when R1 and R3 are both H.
An INDEPENDENT CLAIM is also included for the preparation of (I).
ACTIVITY - Cytostatic. 3-(3,4-Dihydroxyphenyl)-8H-thieno(2,3-b)pyrrolizin-8-one had IC50 values of 356 and 222 nM respectively against P388 and L1210 murine leukemia cells and 122, 33 and 22 nM respectively against A549, KB-3-1 and KB-A1 human solid tumor cells.
MECHANISM OF ACTION - None given.
USE - (I) are anticancer agents especially useful for treating solid tumors.
Dwg.0/0

L81 ANSWER 23 OF 23 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1994-343271 [43] WPIX
DOC. NO. CPI: C1994-156328
TITLE: Pyrrolo pyrazine derivatives having activity on 5-HT3 receptors - useful for treating anxiety, depression, migraine, pain, etc..
DERWENT CLASS: B02
INVENTOR(S): ADAM, G; DELAGRANGE, P; **LANCELOT, J**; PRUNIER, H; **RAULT, S**; **RENARD, P**; ROBBA, M
PATENT ASSIGNEE(S): (ADIR) ADIR & CIE
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 623620	A1	19941109	(199443)*	FR	32
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
FR 2704547	A1	19941104	(199444)		
AU 9461873	A	19941103	(199501)		
CA 2122290	A	19941031	(199505)	FR	
JP 06340666	A	19941213	(199509)		41
NZ 260425	A	19950427	(199522)		
ZA 9402964	A	19950426	(199522)		41
AU 671199	B	19960815	(199641)		
US 5599812	A	19970204	(199711)		10
EP 623620	B1	19980909	(199840)	FR	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
DE 69413112	E	19981015	(199847)		
ES 2123728	T3	19990116	(199909)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 623620	A1	EP 1994-400881	19940425

FR 2704547	A1	FR 1993-5109	19930430
AU 9461873	A	AU 1994-61873	19940428
CA 2122290	A	CA 1994-2122290	19940427
JP 06340666	A	JP 1994-127963	19940502
NZ 260425	A	NZ 1994-260425	19940429
ZA 9402964	A	ZA 1994-2964	19940429
AU 671199	B	AU 1994-61873	19940428
US 5599812	A	US 1994-235426	19940429
EP 623620	B1	EP 1994-400881	19940425
DE 69413112	E	DE 1994-613112	19940425
		EP 1994-400881	19940425
ES 2123728	T3	EP 1994-400881	19940425

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 671199	B	Previous Publ.	AU 9461873
DE 69413112	E	Based on	EP 623620
ES 2123728	T3	Based on	EP 623620

PRIORITY APPLN. INFO: FR 1993-5109 19930430

AN 1994-343271 [43] WPIX

AB EP 623620 A UPAB: 19981021

Pyrrolo pyrazine derivs. of formula (I), their optical isomers and acid addition salts are new. R1=R2-N-R3. R2 and R3 form with the N atom a group selected from (substd.) piperazine, (substd.) piperidine, (substd.) pyrrolidine, (alkyl substd.) morpholine, etc; A forms with the 2 indicated C atoms a benzo, pyrido, pyrazino, or pyrimidino ring and is opt. substd. by alkyl, OH, alkoxy, etc.

USE - The compounds act on 5-HT3 receptors and are useful in the treatment of anxiety, depression, stress, psychoses, schizophrenia, CNS disorders, migraine, memory failure, behavioural disorders, eating disorders, alcoholism, pain, and as anti-emetics.

Dwg.0/0

ABEQ US 5599812 A UPAB: 19970313

Cpds. of formula (I) are new. R1 = N(R2)(R3);N(R2)(R3) =
piperazine,
piperidine, or
pyrrolidine,
(all opt. substd.),
morpholine (opt. substd. by one more alkyl groups),
tetrahydropyridine,
thiomorpholine,
a 5- to 12-membered azaspiro (opt. substd. by one or more alkyl or oxo groups),
a 7- to 12-membered mono- or bicyclic azacycloalkyl optionally including, in its skeleton, to 1 or 2 additional heteroatoms chosen from oxygen, sulphur, and nitrogen,
a 7- to 12-membered mono- or bicyclic azacycloalkyl, substd. by one or more alkyl or oxo groups, opt. including, in its skeleton, to 1 or 2 additional heteroatoms chosen from O, S or N,
-NH-(CH2)k-NH2; k = 2-4,
and a substituted group -NH-(CH2)k-NH2 in which k is as defined above,
and A forms, with the 2 carbon atoms to which it is bonded, a ring chosen from benzo, pyrido, pyrazino and pyrimidino; A being unsubstituted or substituted by one or more radicals chosen from:
alkyl,
hydroxyl,

alkoxy,
acyl,
alkoxycarbonyl,
halogen,
trifluoromethyl,
-(CH2)m-phenyl and -O-(CH2)m-phenyl in which the phenyl ring is itself unsubstituted or substituted by one or more radicals chosen from halogen, alkyl, alkoxy, hydroxyl and trifluoromethyl; and m represents 0 or 1 to 4,
-(CH2)m-piperazine in which the piperazine group is itself substituted or unsubstituted and m is as defined above,
provided that if A forms, with the 2 carbon atoms to which it is bonded, a benzo ring, then R2 and R3 cannot form, with the nitrogen atom which carries them, piperazine which is unsubstituted or substituted by alkyl, phenyl or alkyl-substituted phenyl, morpholine or aminoalkylamines,
it being understood that the term ''substituted'', as it relates to the piperazine, piperidine, pyrrolidine and -NH-(CH2)k-NH2 groups, means that these groups can be substituted by one or more halogen, hydroxyl, oxo, R4 radicals or -C(O)-(R4)

with R4 being chosen from:
alkyl,
alkoxy,
alkenyl which is unsubstituted or substituted by a phenyl which is itself unsubstituted or substituted by one or more radicals chosen from halogen, alkyl, alkoxy, hydroxyl and trifluoromethyl, -(CH2)n-R5 or -(CH2)n'-C(O)-R5,

where n = 0-5, n'= 1-5, R5 = phenyl, benzhydryl, thienyl, pyrrolyl, pyrrolidinyl, furyl, pyrimidinyl, pyridyl, methylenedioxyphenyl, ethylenedioxyphenyl, naphthyl, quinolyl, isoquinolyl, cycloalkyl and dicycloalkylmethyl; the term ''cycloalkyl'' meaning a 3- to 12-membered mono- or bicyclic group, it being possible for these R5 radicals themselves to be substituted by one or more of radicals chosen from halogen, trifluoromethyl, carboxyl, hydroxyl, alkyl and alkoxy,
and (CH2)n'-R6 where n' is as defined above and R6 represents a group chosen from carboxyl, alkoxycarbonyl, amino, alkylamino, dialkylamino, -SO2N(R7)(R8) and -CON(R7)(R8) in which R7 and R8 represent, each independently of the other, a hydrogen atom or an alkyl group,
its optical isomers,
and its addition salts with a pharmaceutically acceptable acid or base,
it being understood that, except when otherwise specified,
the terms ''alkyl'', ''alkoxy'' and ''acyl'' represent linear or branched groups having from 1 to 6 carbon atoms, inclusive,
and the term ''alkenyl'' represents a linear or branched unsaturated group having from 2 to 6 carbon atoms, inclusive.
Dwg.0/0

=> □

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STRUCTURE FILE UPDATES: 18 JUL 2006 HIGHEST RN 894196-03-3
DICTIONARY FILE UPDATES: 18 JUL 2006 HIGHEST RN 894196-03-3

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http://www.cas.org/ONLINE/UG/regprops.html

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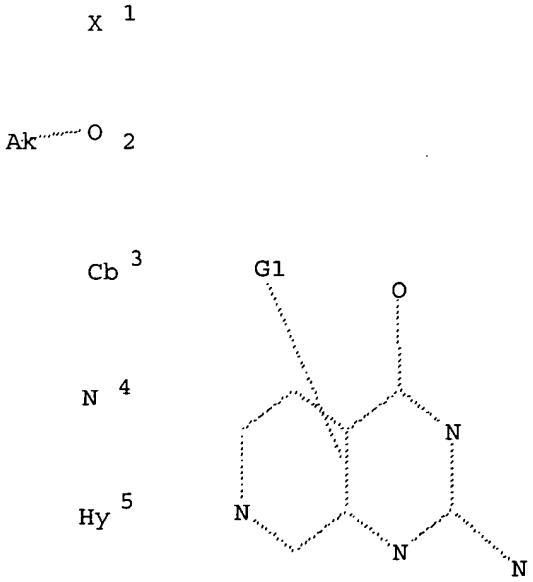
L14 STR



G1 [@1],[@2],[@3],[@4],[@5]

Structure attributes must be viewed using STN Express query preparation.
L16 29 SEA FILE=REGISTRY SSS FUL L14
L42 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

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FILE LAST UPDATED: 18 Jul 2006  (20060718/ED)

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L14             STR
L16           29 SEA FILE=REGISTRY SSS FUL L14
L42            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16

=> s L42 not L79
L83            3 L42 NOT L79

=> file babs
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L41            1 SEA FILE=BABS ABB=ON  PLU=ON  5564377/BABSAN


=> file beilstein
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FILE COVERS 1771 TO 2006.
*** FILE CONTAINS  9,606,495 SUBSTANCES ***

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separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For mo detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

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* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *
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*** PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.**

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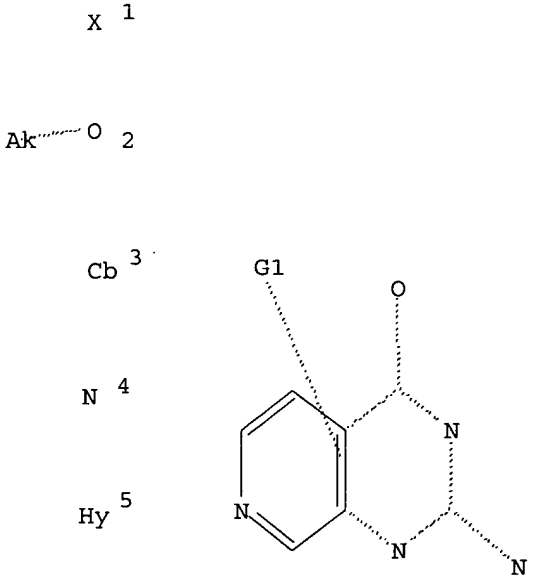
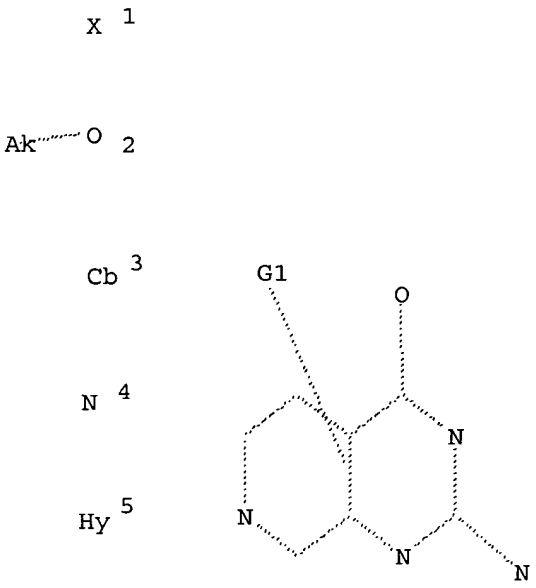
=> d stat que L22
L5 STR



G1 [@1],[@2],[@3],[@4],[@5]

Structure attributes must be viewed using STN Express query preparation.
L7 16 SEA FILE=REGISTRY SSS FUL L5
L14 STR



G1 [@1], [@2], [@3], [@4], [@5]

Structure attributes must be viewed using STN Express query preparation.

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L17           13 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 NOT L7
L18            3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L17
L21            8 SEA FILE=BEILSTEIN SSS FUL L14
L22            1 SEA FILE=BEILSTEIN ABB=ON  PLU=ON  L21 NOT L18
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→ compounds that have CAPlus references

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FILE LAST UPDATED:          14 JUL 2006      <20060714/UP>
MOST RECENT DERWENT UPDATE:     200645        <200645/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

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http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS
    INDEX ENHANCEMENTS PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<
'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d stat que L39
L14             STR
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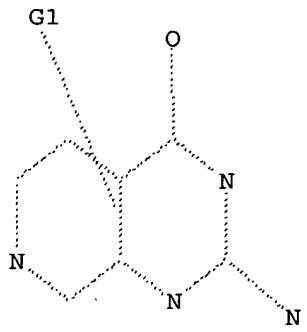
X 1

Ak O 2

Cb 3

N 4

Hy 5



G1 [@1],[@2],[@3],[@4],[@5]

Structure attributes must be viewed using STN Express query preparation.

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L37           2 SEA FILE=WPIX ABB=ON  PLU=ON  (RAEA00/DCN OR RAEA01/DCN OR
                RAEA02/DCN OR RAEA03/DCN OR RAEA04/DCN OR RAEA05/DCN OR
                RAEA07/DCN OR RAEA08/DCN OR RAE9ZS/DCN OR RAE9ZT/DCN OR
                RAE9ZU/DCN OR RAE9ZV/DCN OR RAE9ZW/DCN OR RAE9ZX/DCN OR
                RAE9ZY/DCN OR RAFSCY/DCN)
L38           2 SEA FILE=WPIX ABB=ON  PLU=ON  (902542-0-0-0/DCRE OR 902543-0-0-
                0/DCRE OR 902544-1-0-0/DCRE OR 902544-2-0-0/DCRE OR 902546-0-0-
                0/DCRE OR 902547-0-0-0/DCRE OR 902548-1-0-0/DCRE OR 902548-2-0-
                0/DCRE OR 902550-1-0-0/DCRE OR 902551-0-0-0/DCRE OR 902552-1-0-
                0/DCRE OR 902552-2-0-0/DCRE OR 902553-0-0-0/DCRE OR 902557-0-0-
                0/DCRE OR 902558-0-0-0/DCRE OR 976436-1-0-0/DCRE)
L39           2 SEA FILE=WPIX ABB=ON  PLU=ON  (L36 OR L37 OR L38)

=> s L39 not L80
L84           1 L39 NOT L80
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→ pruned with author search

```
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FILE CONTENT: 1961-PRESENT VOL 145 ISS 1 (20060714/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US   2006118302 08 JUN 2006
```

DE 102004053653 04 MAY 2006
EP 1653548 03 MAY 2006
JP 2006112980 27 APR 2006
WO 2006053912 26 MAY 2006
GB 2419594 03 MAY 2006
FR 2877004 28 APR 2006
RU 2275374 27 APR 2006
CA 2518664 10 MAR 2006

Expanded G-group definition display now available.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

=> d stat que L30
L5 STR

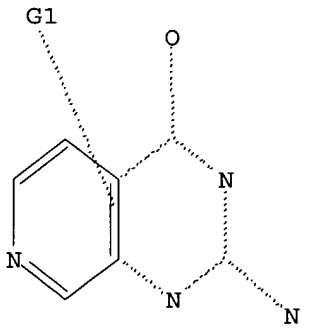
X 1

Ak O 2

Cb 3

N 4

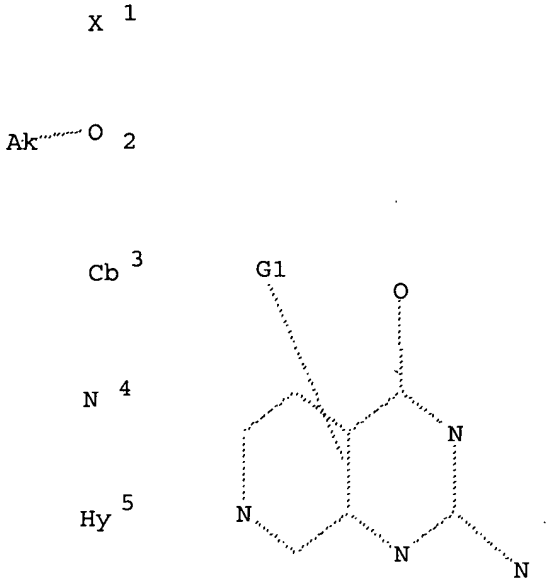
Hy 5



G1 [@1], [@2], [@3], [@4], [@5]

note:
← search query for MARPAT is narrower than for other files

Structure attributes must be viewed using STN Express query preparation.
L14 STR



G1 [@1],[@2],[@3],[@4],[@5]

Structure attributes must be viewed using STN Express query preparation.
L28 49 SEA FILE=MARPAT SSS FUL L14
L30 24 SEA FILE=MARPAT SUB=L28 SSS FUL L5

100.0% PROCESSED 30 ITERATIONS 24 ANSWERS
SEARCH TIME: 00.00.01

=> s L30 not L68
L85 23 L30 NOT L68 → printed with author search

=> => dup rem L83 L84 L41 L85 L22
DUPLICATE IS NOT AVAILABLE IN 'BEILSTEIN'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
FILE 'HCAPLUS' ENTERED AT 11:35:09 ON 19 JUL 2006
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PROCESSING COMPLETED FOR L83
PROCESSING COMPLETED FOR L84
PROCESSING COMPLETED FOR L41
PROCESSING COMPLETED FOR L85
PROCESSING COMPLETED FOR L22
L86 26 DUP REM L83 L84 L41 L85 L22 (3 DUPLICATES REMOVED)
ANSWERS '1-3' FROM FILE HCAPLUS
ANSWERS '4-25' FROM FILE MARPAT
ANSWER '26' FROM FILE BEILSTEIN

=> d ibib abs hitstr L86 1-3; d ibib abs hit L86 4-25; d ide allref L86 26

L86 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:857326 HCAPLUS
DOCUMENT NUMBER: 141:309639
TITLE: Dipeptidyl peptidase inhibitors
INVENTOR(S): Feng, Jun; Gwaltney, Stephen L.; Kaldor, Stephen W.; Stafford, Jeffrey A.; Wallace, Michael B.; Zhang, Zhiyuan
PATENT ASSIGNEE(S): Syrrx, Inc., USA
SOURCE: PCT Int. Appl., 244 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004087053	A2	20041014	WO 2004-US9217	20040324
WO 2004087053	C2	20041111		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 2004242568	A1	20041202	US 2004-809636	20040324
US 2004242566	A1	20041202	US 2004-809638	20040324
US 2004259870	A1	20041223	US 2004-809637	20040324
US 2005004117	A1	20050106	US 2004-809635	20040324
EP 1608317	A2	20051228	EP 2004-758366	20040324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-457785P P 20030325
WO 2004-US9217 W 20040324

OTHER SOURCE(S): MARPAT 141:309639
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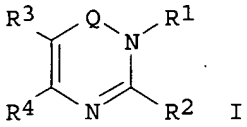


I

AB Dipeptidyl peptidase IV inhibitors I [Q = CO, SO, SO2, C:NR5; R1 = ZR6; Z = moiety providing 1-6 atom separation between R6 and ring; R2 = (substituted)3-7-membered ring; R3,R4 = taken together form a (substituted)5-6-membered ring; R5 = H, (substituted)alkyl, cycloalkyl, etc.; R6 = (substituted)C3-7-cycloalkyl or aryl] are disclosed. Thus, 2-[2-(3-aminopiperidin-1-yl)-6,7-dimethoxy-4-oxo-4H-quinazolin-3-ylmethyl]benzonitrile (I; R1 = 2-cyanophenylmethyl; R2 = 3-aminopiperidin-1-yl; R3,R4 = dimethoxyphenyl) was synthesized. This compound exhibited enhanced stability in rat liver microsomes.

IT **769157-67-7P 769157-79-1P 769157-80-4P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(dipeptidyl peptidase inhibitors)

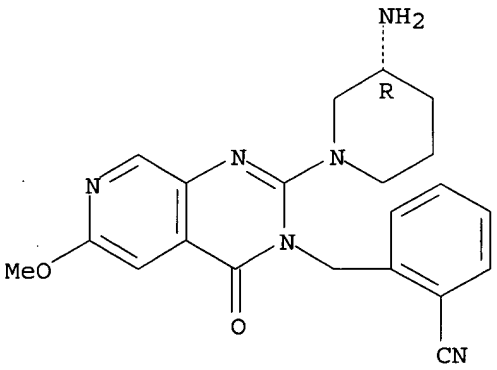
RN 769157-67-7 HCAPLUS

CN Benzonitrile, 2-[[2-[(3R)-3-amino-1-piperidinyl]-6-methoxy-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

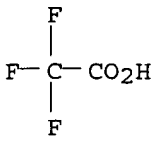
CRN 769157-66-6
CMF C21 H22 N6 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

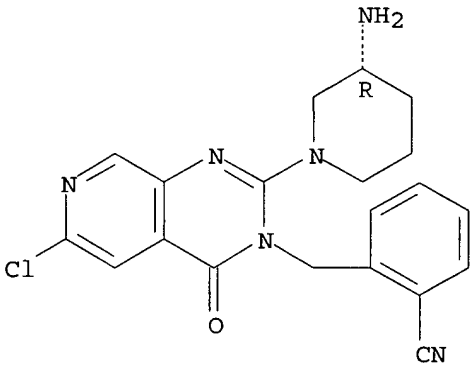


RN 769157-79-1 HCAPLUS
CN Benzonitrile, 2-[[2-[(3R)-3-amino-1-piperidinyl]-6-chloro-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

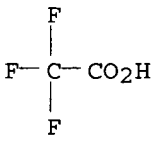
CRN 769157-78-0
CMF C20 H19 Cl N6 O

Absolute stereochemistry.



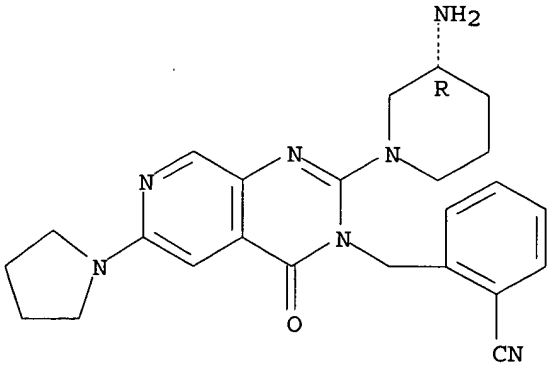
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 769157-80-4 HCAPLUS
CN Benzonitrile, 2-[[2-[(3R)-3-amino-1-piperidinyl]-4-oxo-6-(1-pyrrolidinyl)pyrido[3,4-d]pyrimidin-3(4H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L86 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 1985:113414 HCAPLUS
DOCUMENT NUMBER: 102:113414
TITLE: Synthesis and reactions of 2,3-diamino-4(3H)-pyrimidinones and 3-amino-2-hydrazino-4(3H)-pyrimidinones. I
AUTHOR(S): Hlavka, Joseph J.; Bitha, Panayota; Lin, Yang I.; Strohmeyer, Timothy
CORPORATE SOURCE: Med. Res. Div., Am. Cyanamid Co., Pearl River, NY, 10965, USA
SOURCE: Journal of Heterocyclic Chemistry (1984), 21(5), 1537-41
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 102:113414
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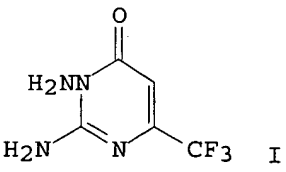


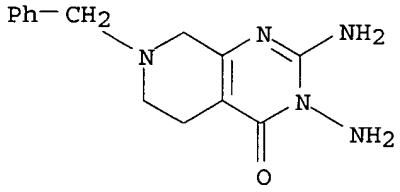
I

AB A series of new 2,3-diamino-4-pyrimidinones and 3-amino-2-hydrazino-4-pyrimidinones were synthesized by the reactions of β-ketoesters with amino or diaminoguanidines. E.g., refluxing aminoguanidine bicarbonate with CF3COCH2CO2Et in BuOH gave 45% pyrimidine I.

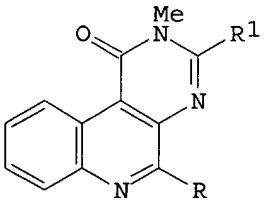
IT **95095-61-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 95095-61-7 HCAPLUS

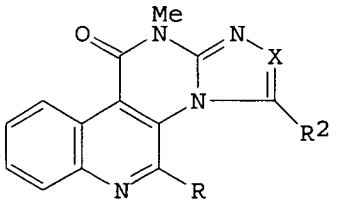
CN Pyrido[3,4-d]pyrimidin-4(3H)-one, 2,3-diamino-5,6,7,8-tetrahydro-7-(phenylmethyl)- (9CI) (CA INDEX NAME)



L86 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:593248 HCAPLUS
DOCUMENT NUMBER: 91:193248
TITLE: Polyaza steroids. II. 1,2,4-triazolo[3',4':2,3]pyrimido[4,5-c]quinolin 11(12H)ones, imidazo[2',1':2,3]pyrimido[4,5-c]quinolin-11(12H)ones and 2,3-dihydroimidazo[2',1':2,3]pyrimido[4,5-c]quinolin-11(12H)ones
AUTHOR(S): Lalezari, I.; Sadeghi-Milani, S.
CORPORATE SOURCE: Coll. Pharm., Tehran Univ., Teheran, Iran
SOURCE: Journal of Heterocyclic Chemistry (1979), 16(4), 707-10
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



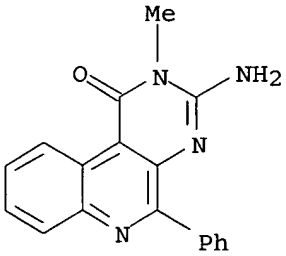
I



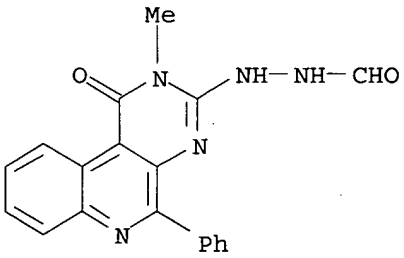
II

AB 2-Substituted quinoline-3,4-dicarboxylic acids were converted in several steps to pyrimido[4,5-c]quinolinones I (R = Me, Ph; R1 = e.g. MeS, NHNH2, NHNHCOH), which were further converted to title polyazasteroids II (X = N, R = Me, Pr, Ph; R2 = H, Me, Et) and II (X = CH; same R, R2). Treating I (R1 = NHNH2) with HONO gave only I (R1 = N3) and not the tetrazolo analog of II (X = N).

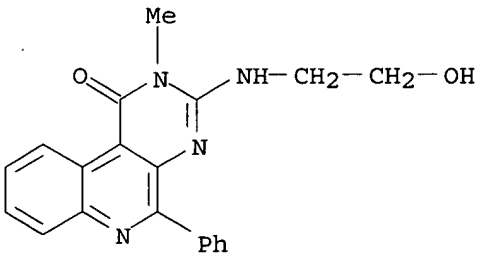
IT **71881-56-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with chloroacetaldehyde)
RN 71881-56-6 HCAPLUS
CN Pyrimido[4,5-c]quinolin-1(2H)-one, 3-amino-2-methyl-5-phenyl- (9CI) (CA INDEX NAME)



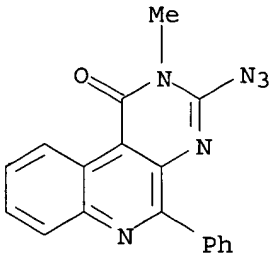
IT **71881-50-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cyclization. of)
RN 71881-50-0 HCAPLUS
CN Hydrazinecarboxaldehyde, 2-(1,2-dihydro-2-methyl-1-oxo-5-phenylpyrimido[4,5-c]quinolin-3-yl)- (9CI) (CA INDEX NAME)



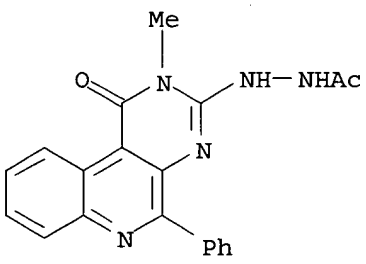
IT **71881-59-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclodehydration of)
RN 71881-59-9 HCAPLUS
CN Pyrimido[4,5-c]quinolin-1(2H)-one, 3-[(2-hydroxyethyl)amino]-2-methyl-5-phenyl- (9CI) (CA INDEX NAME)



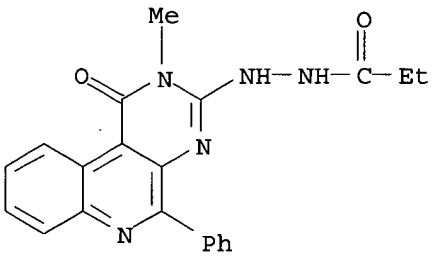
IT **71881-53-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)
RN 71881-53-3 HCAPLUS
CN Pyrimido[4,5-c]quinolin-1(2H)-one, 3-azido-2-methyl-5-phenyl- (9CI) (CA INDEX NAME)



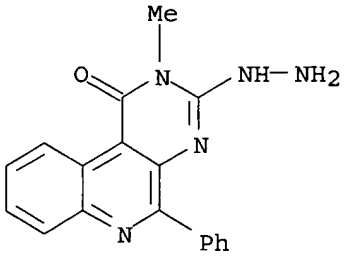
IT **71881-78-2P 71881-79-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 71881-78-2 HCAPLUS
CN Acetic acid, 2-(1,2-dihydro-2-methyl-1-oxo-5-phenylpyrimido[4,5-c]quinolin-3-yl)hydrazide (9CI) (CA INDEX NAME)



RN 71881-79-3 HCAPLUS
CN Propanoic acid, 2-(1,2-dihydro-2-methyl-1-oxo-5-phenylpyrimido[4,5-c]quinolin-3-yl)hydrazide (9CI) (CA INDEX NAME)



IT **71881-43-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, acylation and reaction with nitrous acid)
RN 71881-43-1 HCAPLUS
CN Pyrimido[4,5-c]quinoline-1,3(2H,4H)-dione, 2-methyl-5-phenyl-, 3-hydrazone (9CI) (CA INDEX NAME)



46

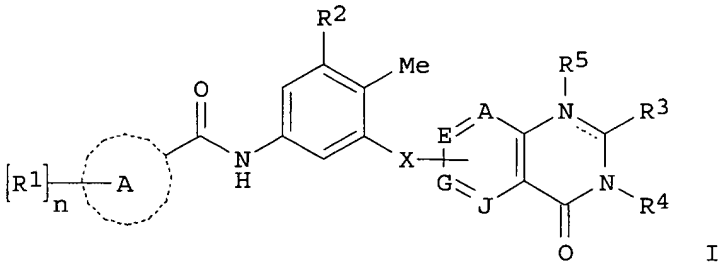
L86 ANSWER 4 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 144:292772 MARPAT
TITLE: Preparation of quinazolinone derivatives as B-Raf inhibitors
INVENTOR(S): Aquila, Brian; Dakin, Les; Ezhuthachan, Jayachandran; Lee, Stephen; Lyne, Paul; Pontz, Timothy; Zheng, Xiaolan
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006024834	A1	20060309	WO 2005-GB3334	20050826

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-605762P 20040831
GI



I

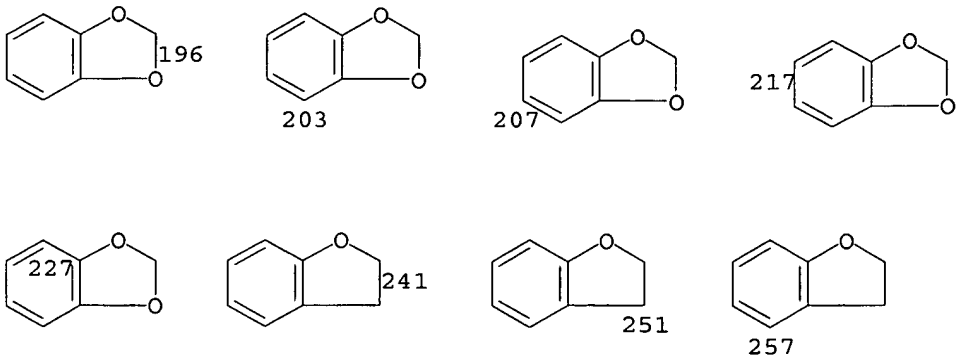
AB The title compds. I [ring A carbocyclyl, heterocyclyl; R1 = halo, nitro, cyano, etc.; n = 0-4; R2 = H, halo, nitro, etc.; X = NR15, O; one of A, E, G and J is C which is attached to X, and the other three are selected from CR16 or N; R3, R16 = H, halo, nitro, etc.; R4, R5, R15 = H, alkyl, alkanoyl, etc.] which possess B-Raf inhibitory activity and are accordingly useful for their anti cancer activity and thus in methods of treatment of the human or animal body, were prepared Thus, reacting N-(3-amino-4-methylphenyl)-3-(1-cyano-1-methylethyl)benzamide with 6-bromo-3-methylquinazolin-4(3H)-one (prepns. of the reactants are given) in the presence of Pd2(dba)3, BINAP and tert-BuONa in PhMe afforded 59% 3-(1-cyano-1-methylethyl)-N-{4-methyl-3-[(3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino]phenyl}benzamide. The compds. I showed IC50 of <30 μM when tested in B-Raf in vitro ELISA assay (specific IC50 values were given for representative compds. I). The invention also relates to processes for the manufacture of compds. I, to pharmaceutical compns. containing them and to their use in the manufacture of medicaments of use in the production of an anti-cancer effect in a warm blooded animal such as man.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1

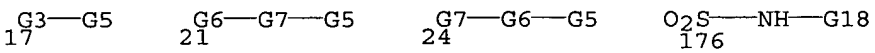
G29——G10

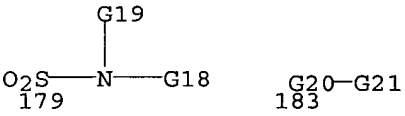
G1 = carbocycle <containing 3-12 C, mono- or bicyclic> (opt. substd. by (up to 4) G2) / heterocycle <containing 4-12 atoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic> (opt. substd. by (up to 4) G2) / heterocycle <containing 1 or more N, attached through 1 or more N> (opt. substd. by 1 or more G8) / (Specifically claimed: 392 / thienyl / pyridyl / thiazolyl / isoxazolyl / furyl / 196 / 203 / 207 / 217 / 227 / pyrazolyl (opt. substd. by 1 or more G22) / indolyl / 241 / 251 / 257 / 261 / 271 / 281 / 289 / 299 / 311 / 321 / 331 / 341 / pyrimidinyl / 410 / 425 / 435 / 446 / 457)



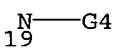
G2 = R / F / Cl / Br / I / NO2 / CN / OH / NH2 / CO2H / CONH2 / SH / SO2NH2 / alkyl <containing 1-6 C> (opt. substd.) / alkenyl <containing 2-6 C> (opt. substd.) / alkynyl <containing 2-6 C> (opt. substd.) / alkoxy <containing 1-6 C> (opt. substd.) / CHO (opt. substd.) / alkylcarbonyl <containing 1-5 C> (opt. substd.) / OCHO (opt. substd.) / alkylcarbonyloxy <containing 1-5 C> (opt. substd.) / alkylamino <containing 1-6 C> (opt. substd.) /

dialkylamino <each alkyl containing 1-6 C> (opt. substd.) / NHCHO / alkylcarbonylamino <containing 1-5 C> (opt. substd.) / alkylaminocarbonyl <containing 1-6 C> (opt. substd.) / dialkylaminocarbonyl <each alkyl containing 1-6 C> (opt. substd.) / 183 / alkoxycarbonyl <containing 1-6 C> (opt. substd.) / alkylaminosulfonyl <containing 1-6 C> (opt. substd.) / dialkylaminosulfonyl <each alkyl containing 1-6 C> (opt. substd.) / alkylsulfonylamino <containing 1-6 C> (opt. substd.) / 17 / 21 / 24 / 176 / 179 / carbocycle <containing 3-12 C, mono- or bicyclic> (opt. substd.) / heterocycle <containing 4-12 atoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic> (opt. substd.) / heterocycle <containing 1 or more N, attached through 1 or more N> (opt. substd. by 1 or more G8)

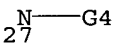




G3 = O / NH / 19 / C(O) / S / S(O) / SO2



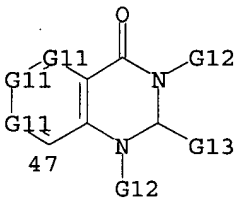
G4 = alkoxycarbonyl <containing 1-6 C> (opt. substd.) / alkyl <containing 1-6 C> (opt. substd.)
G5 = carbocycle <containing 3-12 C, mono- or bicyclic> (opt. substd.) / heterocycle <containing 4-12 atoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic> (opt. substd.)
G6 = C(O) / SO2
G7 = NH / 27

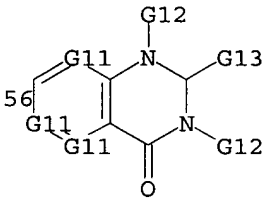


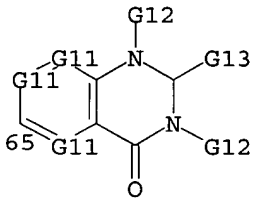
G8 = alkyl <containing 1-6 C> / CHO / alkylcarbonyl <containing 1-5 C> / alkylsulfonyl <containing 1-6 C> / alkoxycarbonyl <containing 1-6 C> / CONH2 / alkylaminocarbonyl <containing 1-6 C> / dialkylaminocarbonyl <each alkyl containing 1-6 C> / CH2Ph / CO2CH2Ph / COPh / SO2Ph
G9 = H / F / Cl / Br / I / NO2 / CN / OH / NH2 / CO2H / CONH2 / SH / SO2NH2 / alkyl <containing 1-6 C> (opt. substd.) / alkenyl <containing 2-6 C> (opt. substd.) / alkynyl <containing 2-6 C> (opt. substd.) / alkoxy <containing 1-6 C> (opt. substd.) / CHO (opt. substd.) / alkylcarbonyl <containing 1-5 C>

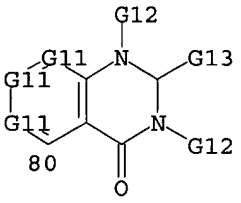
(opt. substd.) / OCHO (opt. substd.) /
alkylcarbonyloxy <containing 1-5 C> (opt. substd.) /
alkylamino <containing 1-6 C> (opt. substd.) /
dialkylamino <each alkyl containing 1-6 C> (opt. substd.) /
NHCHO / alkylcarbonylamino <containing 1-5 C>
(opt. substd.) / alkylaminocarbonyl <containing 1-6 C>
(opt. substd.) / dialkylaminocarbonyl <each alkyl containing
1-6 C> (opt. substd.) / 185 / alkoxycarbonyl <containing 1-6
C> (opt. substd.) / alkylaminosulfonyl <containing 1-6 C>
(opt. substd.) / dialkylaminosulfonyl <each alkyl containing
1-6 C> (opt. substd.) / alkylsulfonylamino <containing 1-6 C>
(opt. substd.) / carbocycle <containing 3-12 C,
mono- or bicyclic> (opt. substd.) /
heterocycle <containing 4-12 atoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
mono- or bicyclic> (opt. substd.) / 37 / 39 / 42 /
heterocycle <containing 1 or more N,
attached through 1 or more N> (opt. substd. by 1 or more G8)

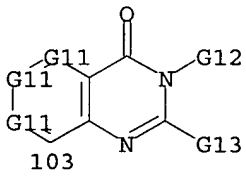
G10 = 47 / 56 / 65 / 80 / **103** / 116 / 129 / 148

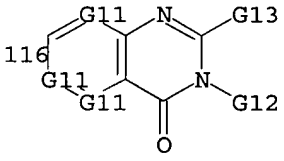


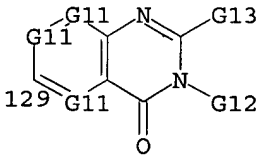


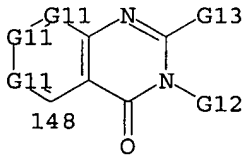






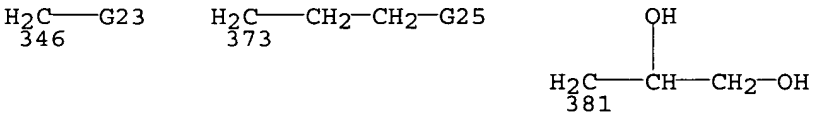




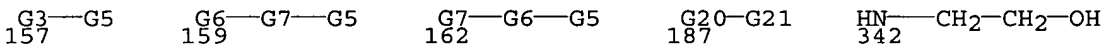


G11 = **N / CH (opt. substd.)**
G12 = H / alkyl <containing 1-6 C> (opt. substd.) /
CHO (opt. substd.) / alkylcarbonyl <containing 1-5 C>
(opt. substd.) / alkylsulfonyl <containing 1-6 C>
(opt. substd.) / alkoxycarbonyl <containing 1-6 C>
(opt. substd.) / CONH2 / **carbocycle <containing 3-12 C,
mono- or bicyclic> (opt. substd.) /**

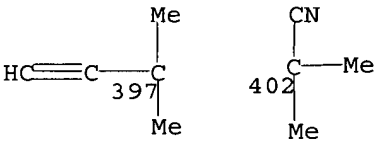
heterocycle <containing 4-12 atoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic> (opt. substd.) / alkylaminocarbonyl <containing 1-6 C> (opt. substd.) / dialkylaminocarbonyl <each alkyl containing 1-6 C> (opt. substd.) / (Specifically claimed: Me / 346 / Et / CH2CH2OH / 373 / 381 / cyclopropyl)



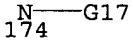
G13 = H / F / Cl / Br / I / **NO2** / CN / OH / NH2 / CO2H / CONH2 / SH / SO2NH2 / alkyl <containing 1-6 C> (opt. substd.) / alkenyl <containing 2-6 C> (opt. substd.) / alkynyl <containing 2-6 C> (opt. substd.) / alkoxy <containing 1-6 C> (opt. substd.) / CHO (opt. substd.) / alkylcarbonyl <containing 1-5 C> (opt. substd.) / OCHO (opt. substd.) / alkylcarbonyloxy <containing 1-5 C> (opt. substd.) / alkylamino <containing 1-6 C> (opt. substd.) / dialkylamino <each alkyl containing 1-6 C> (opt. substd.) / NHCHO / alkylcarbonylamino <containing 1-5 C> (opt. substd.) / alkylaminocarbonyl <containing 1-6 C> (opt. substd.) / dialkylaminocarbonyl <each alkyl containing 1-6 C> (opt. substd.) / 187 / alkoxycarbonyl <containing 1-6 C> (opt. substd.) / alkylaminosulfonyl <containing 1-6 C> (opt. substd.) / dialkylaminosulfonyl <each alkyl containing 1-6 C> (opt. substd.) / alkylsulfonylamino <containing 1-6 C> (opt. substd.) / 157 / 159 / 162 / heterocycle <containing 1 or more N, attached through 1 or more N> (opt. substd. by 1 or more G8) / (Specifically claimed: Me / 342 / NMe2 / SMe)



G14 = H / 397 / 402 / Bu-t

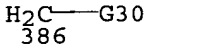


G16 = NH / 174 / O

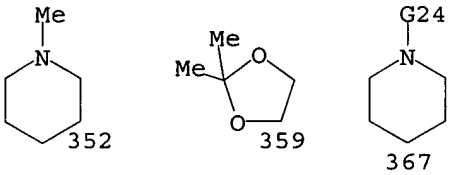


G17 = alkyl <containing 1-6 C> (opt. substd.) / CHO (opt. substd.) / alkylcarbonyl <containing 1-5 C> (opt. substd.) / alkylsulfonyl <containing 1-6 C> (opt. substd.) / alkoxycarbonyl <containing 1-6 C> (opt. substd.) / CONH2 (opt. substd.) /

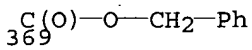
carbocycle <containing 3-12 C, mono- or bicyclic> (opt. substd.) / heterocycle <containing 4-12 atoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic> (opt. substd.) / alkylaminocarbonyl <containing 1-6 C> (opt. substd.) / dialkylaminocarbonyl <each alkyl containing 1-6 C> (opt. substd.) / (Specifically claimed: Me / 386)



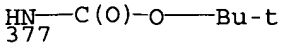
G18 = alkoxy <containing 1-6 C> (opt. substd.)
G19 = alkyl <containing 1-6 C> (opt. substd.)
G20 = S / S(O) / SO2
G21 = alkyl <containing 1-6 C> (opt. substd.)
G22 = alkyl <containing 1-6 C>
G23 = 352 / cyclopropyl / 359 / 367



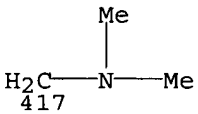
G24 = H / 369



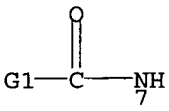
G25 = NH2 / 377 / morpholino



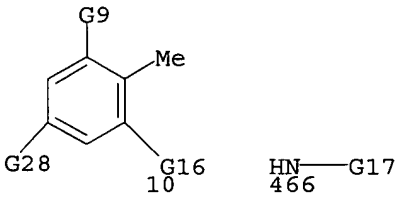
G26 = F / 417



G27 = F / H
G28 = 7 / NH2



G29 = 10 / R <"displaceable group"> / NH2 / 466 / OH



G30 = cyclopropyl / alkyl <containing 2-6 C>
(opt. substd.)
Patent location: claim 1
Note: or pharmaceutically acceptable salts and S-oxides
Note: additional substitution also claimed
Note: additional oxo substitution also claimed
Note: substitution is restricted
Note: also incorporates claim 13, formulae II , V, and VII

L86 ANSWER 5 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 144:274309 MARPAT
TITLE: Preparation of heteroaryl amines as antibacterial agents
INVENTOR(S): Pierau, Sabine; Dale, Glenn
PATENT ASSIGNEE(S): Morphochem Aktiengesellschaft fuer Kombinatorische Chemie, Germany
SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006021448	A1	20060302	WO 2005-EP9204	20050825

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

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DE 102004041163	A1	20060302	DE 2004-102004041163	20040825

PRIORITY APPLN. INFO.: DE 2004-102004041163 20040825
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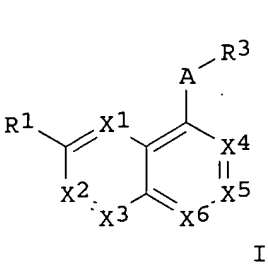

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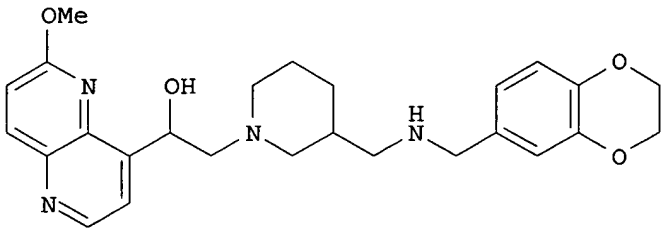
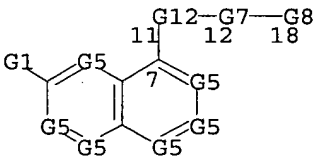


II

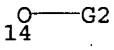
AB The title heteroaryl amines I [wherein X1-X6 = independently N or (un)substituted CH; A = -CH2-CO-, -CH2-SO2-, -NH-SO2-, -CO-NH-, etc.; R1 = H, OH, NH2, halo, (hetero)alkyl, etc.; R3 = (un)substituted piperidinyl, cyclohexyl, morpholino, pyrrolidino, etc.], or pharmacol. acceptable salts, solvates, hydrates, or formulations thereof were prepared as antibacterial agents. For example, II was prepared in a multi-step synthesis. II showed an MIC ≤ 2 μg/mL against at least two organisms.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1



G1 = H / F / Cl / Br / I / **NH2** / SH /
alkyl <containing 1-20 C> (opt. substd. by G3) /
R <"heteroalkyl", containing zero or more B, zero or more N, zero or more O, zero or more P, zero or more S, zero or more Se, zero or more Si (no other heteroatoms), 0 or more double bonds, 0 or more triple bonds, no rings> /
14 / carbocycle <containing 3-14 C, 0 or more double bonds, mono- or polycyclic> (opt. substd. by G4) /
heterocycle <containing 3-14 atoms, zero or more N, zero or more O, zero or more P, zero or more S, zero or more Se, zero or more Si (no other heteroatoms), 0 or more double bonds, mono- or polycyclic> /
(Specifically claimed: OMe)



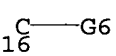
G2 = alkyl <containing 1-20 C> (opt. substd. by G3) /
R <"heteroalkyl", containing zero or more B, zero or more N, zero or more O, zero or more P, zero or more S, zero or more Se, zero or more Si (no other heteroatoms), 0 or more double bonds, 0 or more triple bonds, no rings> /
carbocycle <containing 3-14 C, 0 or more double bonds,

mono- or polycyclic> (opt. substd. by G4) /
heterocycle <containing 3-14 atoms, zero or more N,
zero or more O, zero or more P, zero or more S,
zero or more Se, zero or more Si (no other heteroatoms),
0 or more double bonds, mono- or polycyclic>

G3 = carbocycle <containing 3-14 C,
0 or more double bonds, mono- or polycyclic>

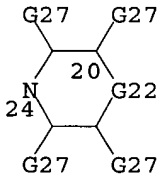
G4 = alkyl <containing 1-20 C> /
alkenyl <containing 2-20 C> / alkynyl <containing 2-20 C> /
R <"heteroalkyl", containing zero or more B, zero or more N,
zero or more O, zero or more P, zero or more S,
zero or more Se, zero or more Si (no other heteroatoms),
0 or more double bonds, 0 or more triple bonds, no rings>

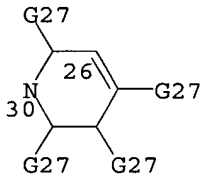
G5 = **N** / **16**

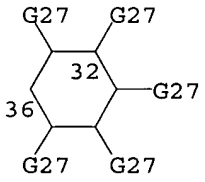


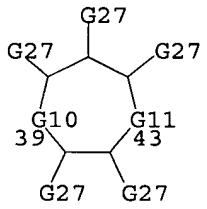
G6 = H / **F** / Cl / Br / I / **OH** / NH2 /
alkyl <containing 1-20 C> / alkenyl <containing 2-20 C> /
alkynyl <containing 2-20 C> / R <"heteroalkyl",
containing zero or more B, zero or more N, zero or more O,
zero or more P, zero or more S, zero or more Se,
zero or more Si (no other heteroatoms),
0 or more double bonds, 0 or more triple bonds, no rings>

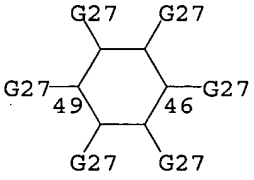
G7 = 24-11 20-18 / 30-11 26-18 / 36-11 32-18 /
39-11 43-18 / 49-11 46-18 / 51-11 53-18 / 56-11 58-18 /
64-11 61-18 / 72-11 69-18

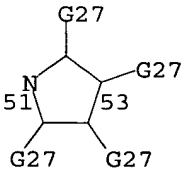


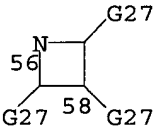


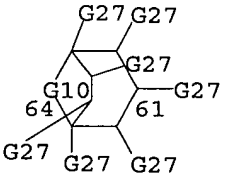


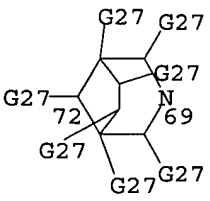






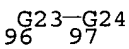




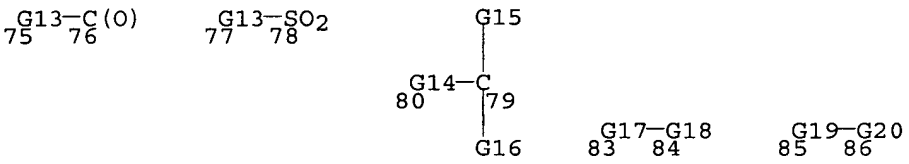


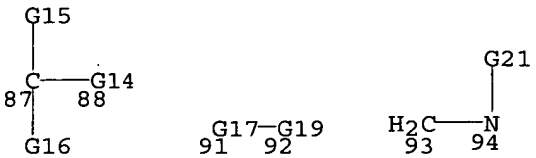
G8 = alkyl <containing 1-20 C> (opt. substd. by G3) /
alkyl <containing 1-20 C> (substd. by 1 or more G9) /

alkenyl <containing 2-20 C> (opt. substd. by 1 or more G9) /
alkynyl <containing 2-20 C> (opt. substd. by 1 or more G9) /
R <"heteroalkyl", containing zero or more B, zero or more N,
zero or more O, zero or more P, zero or more S,
zero or more Se, zero or more Si (no other heteroatoms),
0 or more double bonds, 0 or more triple bonds, no rings> /
aryl <containing 6-14 C, mono- or polycyclic> /
heteroaryl <containing 5-14 atoms, zero or more N,
zero or more O, zero or more P,
zero or more S (no other heteroatoms), mono- or polycyclic> /
carbocycle <containing 3-14 C, 0 or more double bonds,
mono- or polycyclic> (opt. substd. by G4) /
carbocycle <containing 3-14 C, 0 or more double bonds,
mono- or polycyclic> (substd. by 1 or more G9) /
heterocycle <containing 3-14 atoms, zero or more N,
zero or more O, zero or more P, zero or more S,
zero or more Se, zero or more Si (no other heteroatoms),
0 or more double bonds, mono- or polycyclic> /
(Specifically claimed: 96)



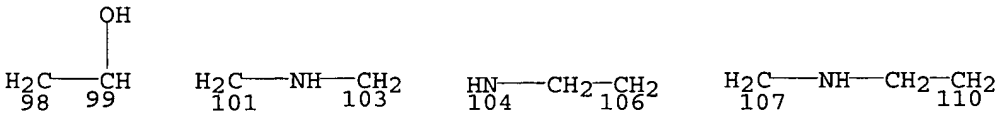
G9 = aryl <containing 6-14 C, mono- or polycyclic> /
heteroaryl <containing 5-14 atoms, zero or more N,
zero or more O, zero or more P,
zero or more S (no other heteroatoms), mono- or polycyclic>
G10 = CH (opt. substd.) / N
G11 = CH / N
G12 = 75-7 76-12 / 77-7 78-12 / 80-7 79-12 /
83-7 84-12 / 85-7 86-12 / 87-7 88-12 / 91-7 92-12 /
(Specifically claimed: 93-7 94-12)

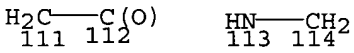




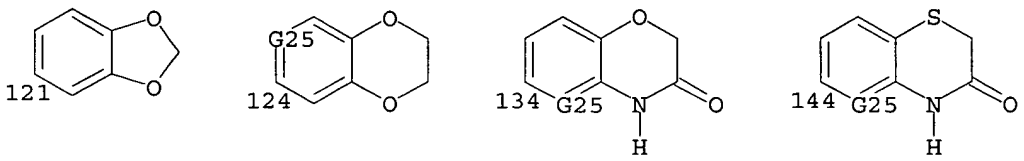
G13 = NH (opt. substd.) / CH2 (opt. substd.)
G14 = CH2 (opt. substd.)
G15 = OH (opt. substd.)
G16 = H / R
G17 = C(O) / CH2 (opt. substd.)
G18 = NH (opt. substd.)
G19 = CH2 (opt. substd.)
G20 = O / S
G21 = alkyl <containing 1-4 C>

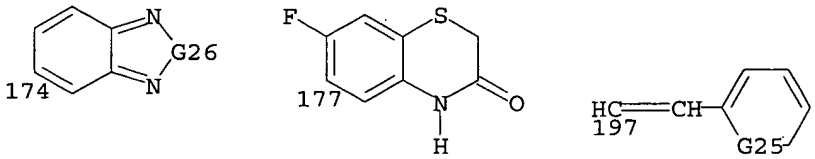
G22 = O / CH2 (opt. substd.)
G23 = alkylene / alkenylene / alkynylene / NH /
R <"heteroalkylene"> / 98-12 99-97 / 101-12 103-97 /
104-12 106-97 / 107-12 110-97 / 111-12 112-97 /
113-12 114-97





G24 = alkyl <containing 1-20 C> (substd. by G3) /
alkyl <containing 1-20 C> (substd. by 1 or more G9) /
alkenyl <containing 2-20 C> (substd. by 1 or more G9) /
alkynyl <containing 2-20 C> (substd. by 1 or more G9) /
R <"heteroalkyl", containing zero or more B, zero or more N,
zero or more O, zero or more P, zero or more S,
zero or more Se, zero or more Si (no other heteroatoms),
0 or more double bonds, 0 or more triple bonds, no rings> /
aryl <containing 6-14 C, mono- or polycyclic> /
heteroaryl <containing 5-14 atoms, zero or more N,
zero or more O, zero or more P,
zero or more S (no other heteroatoms), mono- or polycyclic> /
carbocycle <containing 3-14 C, 0 or more double bonds,
mono- or polycyclic> (opt. substd. by G4) /
heterocycle <containing 3-14 atoms, zero or more N,
zero or more O, zero or more P, zero or more S,
zero or more Se, zero or more Si (no other heteroatoms),
0 or more double bonds, mono- or polycyclic> / 121 / 124 /
134 / 144 / 197 / 174 / 177





G25 = CH / N
G26 = O / S
G27 = H / R
Patent location: claim 1
Note: or pharmacologically acceptable salts, solvates,
hydrates or pharmacologically acceptable

formulation
Note: additional substitution also claimed

L86 ANSWER 6 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 144:150378 MARPAT
TITLE: Preparation of pyrido[2,3-d]pyrimidine-2,4-diones and related compounds as selective dipeptidyl peptidase inhibitors
INVENTOR(S): Feng, Jun; Gwaltney, Stephen L.; Lam, Betty; Zhang, Zhiyuan
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 55 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006014764	A1	20060119	US 2005-183335	20050715
WO 2006019965	A2	20060223	WO 2005-US25070	20050714
WO 2006019965	A3	20060406		

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WO 2006020017	A2	20060223	WO 2005-US25153	20050715

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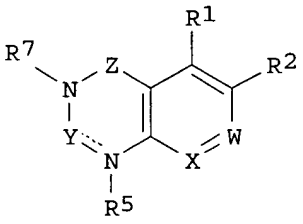
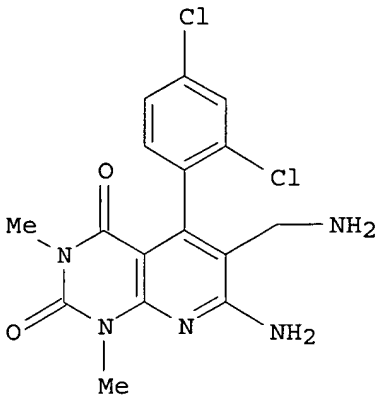
PRIORITY APPLN. INFO.: US 2004-588577P 20040716
GI



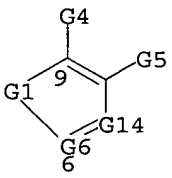
I



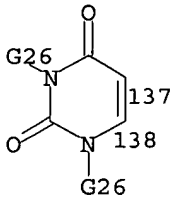
II

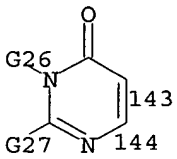
AB Pyrido[2,3-d]pyrimidine-2,4-diones and related compds. (shown as I; variables defined below; e.g. 7-amino-6-aminomethyl-5-(2,4-dichlorophenyl)-1,3-dimethyl-1H-pyrido[2,3-d]pyrimidine-2,4-dione trifluoroacetate (free base shown as II)), pharmaceutical compns., kits and methods are provided for inhibiting DPP-IV and other S9 proteases. Although the methods of preparation are not claimed, prepns. and/or characterization data for .apprx.50 examples of I are included. For example, II was prepared by cyclizing 2-(2,4-dichlorobenzylidene)malononitrile (prepared from 2,4-dichlorobenzaldehyde and malononitrile) with 6-amino-1,3-dimethyluracil followed by reduction with BH3-THF and acidification with TFA. For I: W = CR3 and N; X = CR4 and N; Y = CO, CS, SO, SO2, CR6R6' and C:NR6; Z = CO, CS, SO, SO2, and C:NR6; R1 = (C1-10)alkyl, (C3-12)cycloalkyl, hetero(C3-12)cycloalkyl, aryl(C1-10)alkyl, heteroaryl(C1-5)alkyl, et al.; R2 = amino(C1-6)alkyl, hetero(C3-12)cycloalkyl, hetero(C4-12)bicycloaryl, heteroaryl, and cyano; R5 and R7 = H, halo(C1-10)alkyl, amino, nitro, thio, sulfonamide, (C1-10)alkyl, (C3-12)cycloalkyl, et al.; addnl. details including provisos are given in the claims. Compds. I were tested according to assays for protease inhibition and observed to exhibit selective DPP-IV inhibitory activity. For example, they inhibit DPP-IV activity at concns. that are at least 50 fold less than those concns. required to produce an equiactive inhibition of protease activity for FAPα. The apparent inhibition consts. (Ki) for compds. of the invention, against DPP-IV, were .apprx.10-9 M to .apprx.10-5 M.

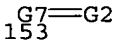
MSTR 1

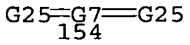


G1 = 153 / 154 / (Specifically claimed: 137-9 138-6 / **143-9 144-6**)

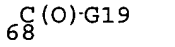


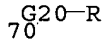


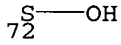


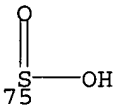


G2 = H / F / Cl / Br / I / alkyl <containing 1-10 C, no H> (substd. by 3 or more G18) / NH2 (opt. substd.) / NO2 / CN / SH / SO2NH2 / alkyl <containing 1-10 C> / carbocycle <containing 3-12 C, non-aromatic> / heterocycle <containing zero or more N, zero or more O, zero or more S, 3-12 C, non-aromatic> / alkyl <containing 1-10 C> (substd. by 1 or more aryl) / alkyl <containing 1-5 C> (substd. by heteroaryl <containing zero or more N, zero or more O, zero or more S>) / aryl <containing 9-12 C, polycyclic> / heteroaryl <containing zero or more N, zero or more O, zero or more S, 4-12 C, polycyclic> / alkyl <containing 1-3 C> (substd. by G22) / 84 / alkylamino <containing 1-10 C> / alkyl <containing 1-10 C> (substd. by NH2 (opt. substd.)) / aryl / heteroaryl <containing zero or more N, zero or more O, zero or more S> / OH / alkoxy / aryloxy / heteroaryloxy <containing zero or more N, zero or more O, zero or more S> / 68 / 70 / 72 / 75



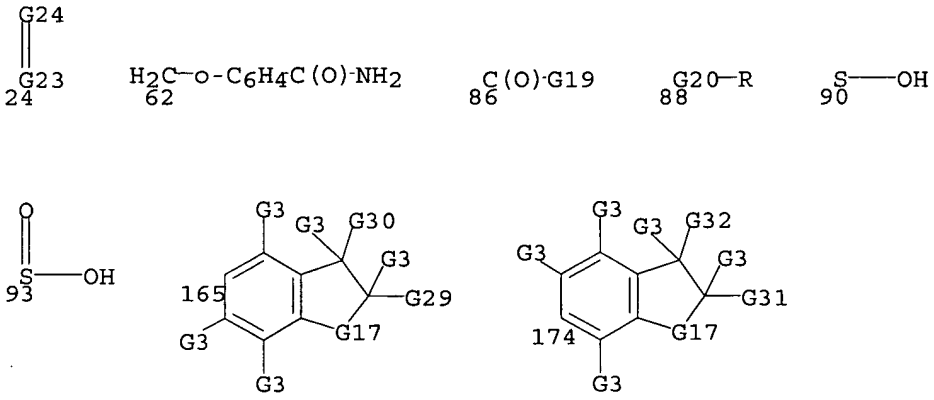




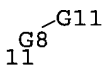


G3 = H / R

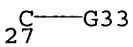
G4 = alkyl <containing 1-10 C> / carbocycle <containing 3-12 C, non-aromatic> / heterocycle <containing zero or more N, zero or more O, zero or more S, 3-12 C, non-aromatic> / alkyl <containing 1-10 C> (substd. by 1 or more aryl) / alkyl <containing 1-5 C> (substd. by heteroaryl <containing zero or more N, zero or more O, zero or more S>) / aryl <containing 9-12 C, polycyclic> / heteroaryl <containing zero or more N, zero or more O, zero or more S, 4-12 C, polycyclic> / alkyl <containing 1-3 C> (substd. by G22) / 24 / NH2 (opt. substd.) / aryl / heteroaryl <containing zero or more N, zero or more O, zero or more S> / OH / alkoxy / aryloxy / heteroaryloxy <containing zero or more N, zero or more O, zero or more S> / alkenyl / alkynyl / CN / 86 / 88 / 90 / 93 / (Specifically claimed: heterocycle <containing 1-4 heteroatoms, up to 1 O, up to 1 S, up to 4 N (no other heteroatoms), 1-4 C, attached through 1 or more C, aromatic, 2 double bonds, 5-membered monocyclic ring> (opt. substd.) / pyridyl (opt. substd. by 1 or more G13) / Ph (opt. substd. by 1 or more G16) / thienyl (opt. substd. by 1 or more G13) / 62 / 165 / 174)



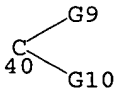
G5 = alkyl <containing 1-6 C>
(substd. by NH2 (opt. substd.)) /
heterocycle <containing zero or more N, zero or more O,
zero or more S, 3-12 C, non-aromatic> /
heteroaryl <containing zero or more N, zero or more O,
zero or more S, 4-12 C, polycyclic> /
heteroaryl <containing zero or more N, zero or more O,
zero or more S> / CN / (Specifically claimed: 11)



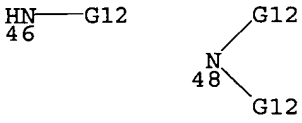
G6 = N / **27**



G7 = heterocycle <containing 2-4 heteroatoms, 2 N,
up to 2 S (no other heteroatoms), 2 or more C,
attached through 2 or more C, 1-2 double bonds,
6-membered monocyclic ring> (opt. substd.)
G8 = 40 / any ring <containing zero or more N,
zero or more O, zero or more S, attached through 1 or more C>
(opt. substd.)

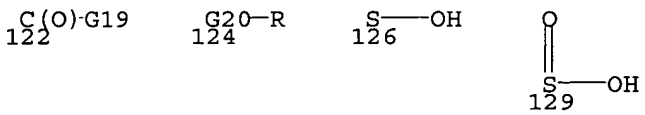


G9 = H / F / Cl / Br / I / alkyl <containing 1-10 C,
no H> (substd. by 3 or more G18) / CN / NO2 / alkyl /
carbocycle <non-aromatic> / alkenyl / alkynyl / aryl /
heteroaryl <containing zero or more N, zero or more O,
zero or more S>
G10 = H / R
G11 = NH2 / 46 / 48 / heterocycle <containing 1 or more
N, zero or more O, zero or more S, attached through 1 N>

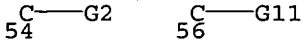


G12 = alkyl <containing 1-10 C, no H>
(substd. by 3 or more G18) / NH2 (opt. substd.) / SH /
alkyl <containing 1-10 C> / carbocycle <containing 3-12 C,
non-aromatic> / heterocycle <containing zero or more N,
zero or more O, zero or more S, 3-12 C, non-aromatic> /
alkyl <containing 1-10 C> (substd. by 1 or more aryl) /
alkyl <containing 1-5 C> (substd. by heteroaryl <containing
zero or more N, zero or more O, zero or more S>) /
aryl <containing 9-12 C, polycyclic> /
heteroaryl <containing zero or more N, zero or more O,
zero or more S, 4-12 C, polycyclic> /
alkyl <containing 1-3 C> (substd. by G22) / 51 / aryl /
heteroaryl <containing zero or more N, zero or more O,
zero or more S> / OH / alkoxy / aryloxy /
heteroaryloxy <containing zero or more N, zero or more O,
zero or more S>

G13 = F / Cl / Br / I / alkyl <containing 1-10 C, no H>
(substd. by 3 or more G18) / CF3 /
alkyl <containing 1-10 C> / alkenyl / alkynyl / aryl /
heteroaryl <containing zero or more N, zero or more O,
zero or more S> / SO2NH2 / alkylsulfonyl / arylsulfonyl /
heteroarylsulfonyl <containing zero or more N,
zero or more O, zero or more S> / aryloxy /
heteroaryloxy <containing zero or more N, zero or more O,
zero or more S> / alkyl (substd. by 1 or more aryl) /
alkyl (substd. by heteroaryl <containing zero or more N,
zero or more O, zero or more S>) /
carbocycle <non-aromatic> / heterocycle <containing zero or
more N, zero or more O, zero or more S, non-aromatic> /
NH2 (opt. substd.) / SH / CN / NO2 / OH / alkoxy / 122 /
124 / 126 / 129

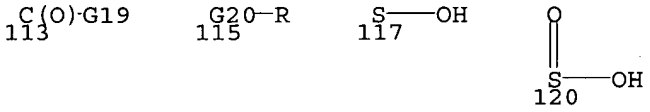


G14 = **N** / 54 / (Specifically claimed: 56)

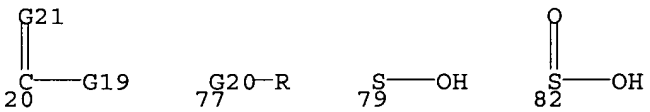


G16 = F / Cl / Br / I / alkyl <containing 1-10 C, no H>
(substd. by 3 or more G18) / CF3 /

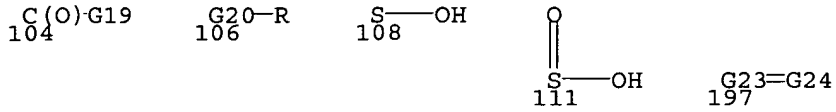
alkyl <containing 1-10 C> / alkenyl / alkynyl / aryl / heteroaryl <containing zero or more N, zero or more O, zero or more S> / SO2NH2 / alkylsulfonyl / arylsulfonyl / heteroarylsulfonyl <containing zero or more N, zero or more O, zero or more S> / aryloxy / heteroaryloxy <containing zero or more N, zero or more O, zero or more S> / alkyl (substd. by 1 or more aryl) / alkyl (substd. by heteroaryl <containing zero or more N, zero or more O, zero or more S>) / carbocycle <non-aromatic> / heterocycle <containing zero or more N, zero or more O, zero or more S, non-aromatic> / NH2 (opt. substd.) / SH / CN / NO2 / OH / alkoxy / 113 / 115 / 117 / 120 / OMe / CO2H / CONH2 / tetrazolyl / CH2NH2 / CH2OH / Ph / tetrazolyl / alkylaminocarbonyl <containing 1-7 C> / alkoxycarbonyl <containing 1-7 C>



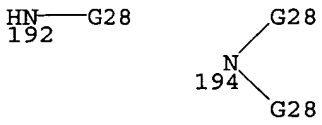
G17 = O / S / NH (opt. substd.)
G18 = F / Cl / Br / I
G19 = H / R
G20 = S(O) / SO2
G21 = O / S
G22 = 20 / 77 / 79 / 82



G23 = carbon chain <containing 1-3 C, saturated> (opt. substd.)
G24 = NH (opt. substd.)
G25 = O / S / NH (opt. substd.)
G26 = H / alkyl <containing 1-10 C> (substd. by 1 or more G18) / NH2 (opt. substd.) / NO2 / SH / SO2NH2 / alkyl <containing 1-10 C> / carbocycle <containing 3-12 C, non-aromatic> / heterocycle <containing zero or more N, zero or more O, zero or more S, 3-12 C, non-aromatic> / alkyl <containing 1-10 C> (substd. by 1 or more aryl) / alkyl <containing 1-5 C> (substd. by heteroaryl <containing zero or more N, zero or more O, zero or more S>) / aryl <containing 9-12 C, polycyclic> / heteroaryl <containing zero or more N, zero or more O, zero or more S, 4-12 C, polycyclic> / alkyl <containing 1-3 C> (substd. by G22) / 197 / aryl / heteroaryl <containing zero or more N, zero or more O, zero or more S> / OH / alkoxy / aryloxy / heteroaryloxy <containing zero or more N, zero or more O, zero or more S> / 104 / 106 / 108 / 111 / (Specifically claimed: Me)



G27 = **NH2** / 192 / 194 / heterocycle <containing 1 or more N, attached through 1 N>



G28 = NH2 (opt. substd.) / alkyl / carbocycle <non-aromatic> / heterocycle <containing zero or more N, zero or more O, zero or more S> / alkyl (substd. by 1 or more aryl) / alkyl (substd. by heteroaryl <containing zero or more N, zero or more O, zero or more S>) / aryl <polycyclic> / heteroaryl <containing zero or more N, zero or more O, zero or more S, polycyclic>

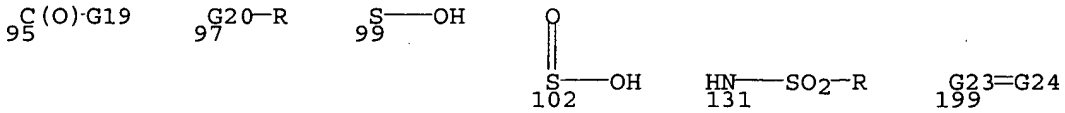
G29 = H / R

G30 = H / R

G31 = H / R

G32 = H / R

G33 = H / **F** / Cl / Br / I / alkyl <containing 1-10 C, no H> (substd. by 3 or more G18) / NH2 (opt. substd.) / NO2 / CN / SH / SO2NH2 / alkyl <containing 1-10 C> / carbocycle <containing 3-12 C, non-aromatic> / heterocycle <containing zero or more N, zero or more O, zero or more S, 3-12 C, non-aromatic> / alkyl <containing 1-10 C> (substd. by 1 or more aryl) / alkyl <containing 1-5 C> (substd. by heteroaryl <containing zero or more N, zero or more O, zero or more S>) / aryl <containing 9-12 C, polycyclic> / heteroaryl <containing zero or more N, zero or more O, zero or more S, 4-12 C, polycyclic> / alkyl <containing 1-3 C> (substd. by G22) / 199 / alkylamino <containing 1-10 C> / alkyl <containing 1-10 C> (substd. by NH2 (opt. substd.)) / aryl / heteroaryl <containing zero or more N, zero or more O, zero or more S> / OH / alkoxy / aryloxy / heteroaryloxy <containing zero or more N, zero or more O, zero or more S> / 95 / 97 / 99 / 102 / 131



G29+G30= bond

G31+G32= bond

Patent location: claim 1

Note: additional substitution and ring formation also claimed

L86 ANSWER 7 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:455888 MARPAT
TITLE: Halogenated coordination compounds preparation and use thereof
INVENTOR(S): Schwaiger, Jochen; Bach, Ingrid; Stoessel, Philipp
PATENT ASSIGNEE(S): Covion Organic Semiconductors G.m.b.H., Germany
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042545	A2	20050512	WO 2004-EP11891	20041021
WO 2005042545	A3	20060105		

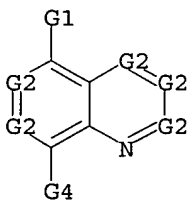
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10351556	A1	20050602	DE 2003-10351556	20031103

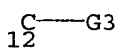
PRIORITY APPLN. INFO.: DE 2003-10351556 20031103
OTHER SOURCE(S): CASREACT 142:455888

AB The invention relates to novel halogenated coordination compds. containing azanaphthalenols/thiols/selenols, of application as functional materials in differing applications within the widest sense of the electronic industry and which comprise organically-bonded halides as reactive groups. The invention further relates to a method for regioselective preparation of said compds. For example, AlL2 (HL = 8-hydroxyquinoline) was brominated with N-bromosuccinimide to give AlL13 (HL1 = 5-bromo-8-hydroxyquinoline) in 99 % yield.

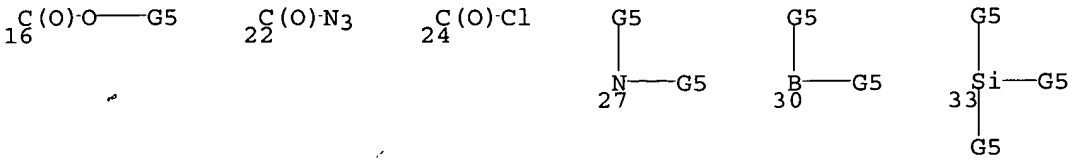
MSTR 1

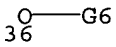


G1 = **Cl** / F / Br / I / H
G2 = **N** / **12**

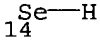


G3 = H / F / Cl / Br / I / CN / CHO / 16 / 22 / 24 / **NO2** / 27 / 30 / 33 / carbon chain <containing 1 or more C> (opt. substd.) / **36**





G4 = OH / SH / 14 / aryl <containing up to 40 C> (opt. substd.) / heteroaryl <containing up to 40 atoms, zero or more O, zero or more S, zero or more N (no other heteroatoms)> (opt. substd.)



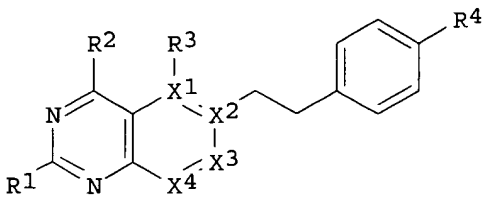
G5 = H / R
G6 = carbon chain <containing 1 or more C> (opt. substd.) / aryl <containing up to 40 C> (opt. substd.) / heteroaryl <containing up to 40 atoms, zero or more O, zero or more S, zero or more N (no other heteroatoms)> (opt. substd.)
G10 = R <"metal"> / (Specifically claimed: Al / Be / B / Ca / Ga / In / Ir / Li / Mg / Zn)
Patent location: claim 1
Note: as complexes with G10
Note: additional ligands and ring formation also claimed
Note: also incorporates claim 13, structure IV

Maybe

L86 ANSWER 8 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:134921 MARPAT
TITLE: Process for synthesizing quinazoline γ-methylene-L-glutamic acid and related antifolates
INVENTOR(S): Wu, Ye; Kochat, Harry
PATENT ASSIGNEE(S): Bionumerik Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005020833	A1	20050127	US 2003-627483	20030725
US 7060825	B2	20060613		

PRIORITY APPLN. INFO.: US 2003-627483 20030725
GI

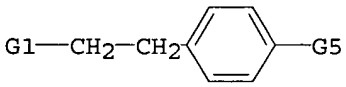


I

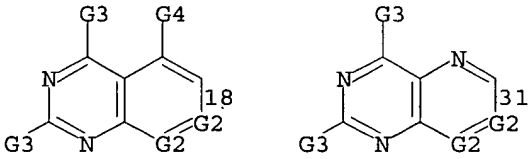
AB The invention relates to a process for synthesizing antifolate compds. I [R1, R3 are individually NH2, alkylamino, OH, alkoxy, keto, alkyl or a protecting group; R3 is H, OH, alkoxy, trifluoromethylalkoxy, halo or alkylthio; R4 is OH, alkoxy or CO-X, where X is OH, alkoxy or an amino acid residue; X1-X4 are each individually carbon or nitrogen] that have com. use as drugs in oncol., inflammatory disease, and other medical fields. Thus, cyclization reaction of 2-amino-5-nitrobenzonitrile with guanidine in the presence of NaOMe afforded 2,4-diamino-6-nitroquinazoline (Q-NO2). The latter is converted to reactive aldehyde Q-CHO in 3 steps starting with reduction to the amine. The 6-formylquinazoline is then coupled to a benzoic acid ester by a modified Horner reaction. Subsequent hydrogenation, saponification, coupling with di-Et γ-methylene-L-glutamate, and saponification afforded p-Q-CH2CH2C6H4CONHCH(CO2H)CH2C(:CH2)CO2H-(S).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

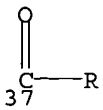
MSTR 1



G1 = **18** / 31



G2 = **CH** / **N**
G3 = **NH2** / alkylamino / dialkylamino / **OH** / alkoxy / 37
/
loweralkyl / R <"nitrogen or oxygen protecting group">

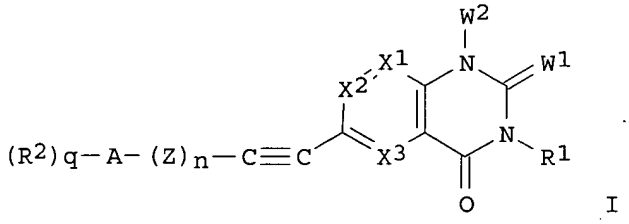


G4 = H / OH / alkoxy / CF3 / **halo** / SH / alkylthio
G5 = H / alkoxy / 40

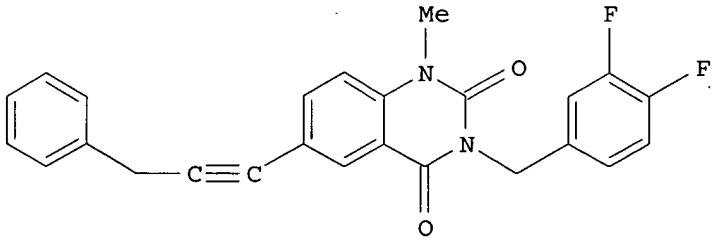
US 2003130278	A1	20030710	US 2002-269197	20021011
US 6962922	B2	20051108		
BR 2002013239	A	20040928	BR 2002-13239	20021011
EP 1465878	A1	20041013	EP 2002-801341	20021011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005509626	T2	20050414	JP 2003-536218	20021011
US 2005245548	A1	20051103	US 2005-148880	20050609

PRIORITY APPLN. INFO.: US 2001-329181P 20011012
WO 2001-EP11824 20011012
US 2002-395441P 20020712
WO 2002-EP8475 20020712
US 2002-269197 20021011
WO 2002-EP12194 20021011

GI



I

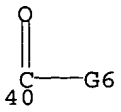


II

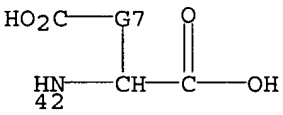
AB The title compds. I [W1 = O, S, (substituted)amino; W2 = H, CF3, (substituted)amino, alkyl, alkenyl, alkynyl, aryl, etc.; W1W2 = heteroalkylene, etc; X1, X2 and X3 = N or (substituted)carbon; n = 0-8; Z = CR3R4, where R3, R4 = H, alkyl, halogen, (substituted)amino, etc.; A = (hetero)aryl or (hetero)cycloalkyl; R1 = H, alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, halogen, cyano, nitro, (substituted)amino, etc.; q = 0-7] were prepared as inhibitors of type-13 matrix metalloprotease. Thus, reaction of 3-(3,4-difluoro-benzyl)-6-iodo-1-methyl-1H-quinazoline-2,4-dione (preparation given) with 3-phenyl-propyne yielded compound II. The IC50 values on MMP-13 of the prepared compds. are all below 10 μM.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1



G6 = OH / alkoxy / R <"amino acid residue"> /
(Example: 42)



G7 = (1-2) CH2
Patent location: claim 1

1

L86 ANSWER 9 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:94063 MARPAT
TITLE: Preparation of new alkynylated quinazoline compounds as MMP-13 inhibitors
INVENTOR(S): Gaudilliere, Bernard; Jacobelli, Henry; Wilson, Michael William; Picard, Joseph Armand
PATENT ASSIGNEE(S): Warner-Lambert Company Llc, USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007469	A1	20040122	WO 2002-EP8475	20020712
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002331362	A1	20040202	AU 2002-331362	20020712
CA 2463159	AA	20030424	CA 2002-2463159	20021011
WO 2003033478	A1	20030424	WO 2002-EP12194	20021011
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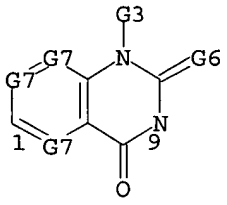
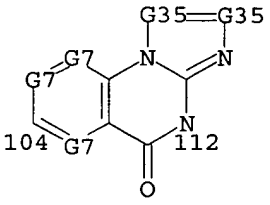
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

G20–G13–G1—G32
18 19 20 21

G1 = **1-19 9-21** / 104-19 112-21





G2 = alkyl <containing 1-6 C> / OH / CN
G3 = H / CF3 / NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> /
alkyl <containing 1-6 C> (opt. substd. by 1 or more G4) /
alkenyl <containing 2-6 C> (opt. substd. by 1 or more G4) /
alkynyl <containing 2-6 C> (opt. substd. by 1 or more G4) /
aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4) /
alkyl <containing 1-6 C> (substd. by 1 or more G30) /
alkyl <containing 1-6 C> (substd. by G31) /
heteroaryl <containing 1-4 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
monocyclic> (opt. substd. by 1 or more G4) /
heterocycle <containing 1-4 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
non-aromatic, 0 or more double bonds,
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G4) / (Specifically claimed: Me)
G4 = halo / NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / CN /
alkyl <containing 1-6 C> (substd. by (3) halo) / 16 / OH /
SH / alkoxy <containing 1-6 C> /
alkylthio <containing 1-6 C>

C(O)-G5
16

G5 = alkyl <containing 1-6 C> / Ph / OH /
alkoxy <containing 1-16 C>
G6 = O / S / **NH** / 13

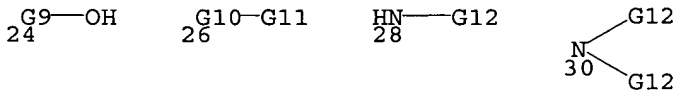
N——G2
13

G7 = **(up to 2) N / 22**

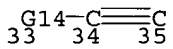
C——G8
22

G8 = H / alkyl <containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / **halo** / CF3 / CN / NO2 / SH / 24

/
26 / NH2 / 28 / 30 / heterocycle <containing 1-2
heteroatoms, 1 or more N, zero or more O (no other
heteroatoms), attached through 1 or more N,
5- to 6-membered monocyclic ring>

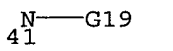


G9 = S / S(O)
G10 = S / S(O) / SO2
G11 = alkyl <containing 1-6 C>
G12 = alkyl <containing 1-6 C> /
alkyl <containing 1-6 C> (substd. by 1 or more aryl
<containing up to 10 C, mono- or bicyclic>)
G13 = ethynylene / 33-18 35-20

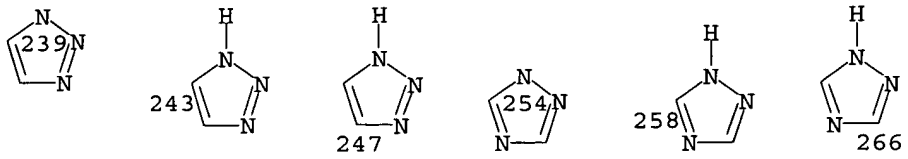


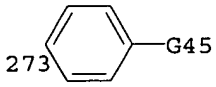
G14 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 36 / 38-18 40-34 /
(Specifically claimed: CH2)

G15 = halo / NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C> /
CO2H / alkoxycarbonyl <containing 1-6 C>
G16 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G17 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G18 = O / S / S(O) / SO2 / NH / 41

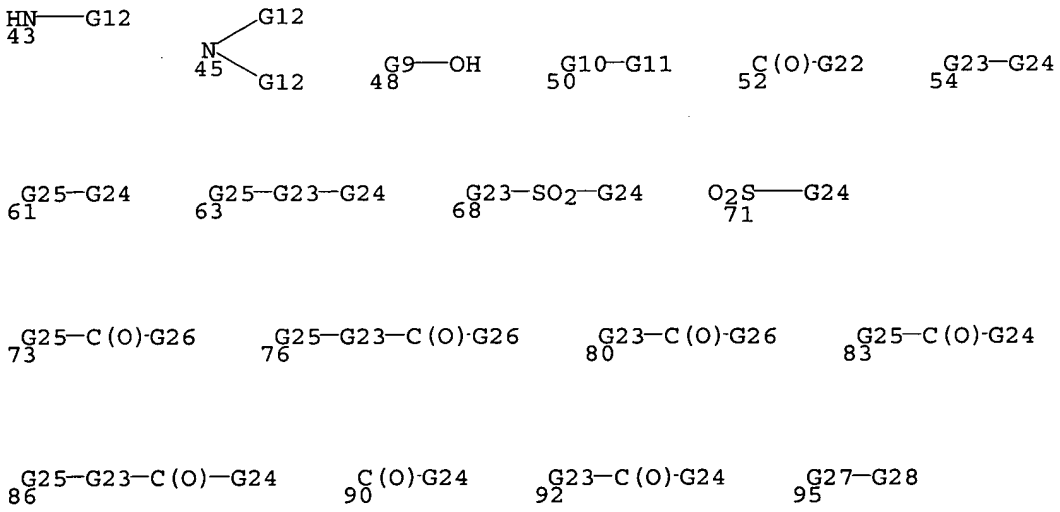


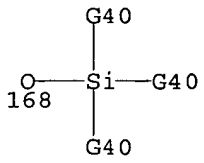
G19 = alkyl <containing 1-6 C>
G20 = carbocycle <containing 8-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
heterocycle <containing 8-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
(Specifically claimed: Ph / imidazolyl / 239 / 243 / 247 /
254 / 258 / 266 / 273)



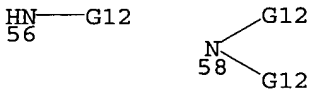


G21 = alkyl <containing 1-6 C> / halo / CN / NO2 / alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 43 / 45 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring> / OH / SH / 48 / 50 / 52 / 54 / 61 / 63 / 68 / 71 / 73 / 76 / CO2H / alkoxycarbonyl <containing 1-6 C> / 80 / 83 / 86 / 90 / 92 / 95 / aryl <containing up to 10 C, mono- or bicyclic> (opt. substd. by (1-4) G29) / heteroaryl <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic> (opt. substd. by (1-4) G29) / heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, mono- or bicyclic, (1) 5- or more membered ring, (1) up to 6-membered ring> (opt. substd. by (1-4) G29) / carbocycle <containing 3-10 C, non-aromatic, 0 or more double bonds, mono- or bicyclic> (opt. substd. by 1 or more G29) / 168

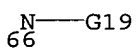




G22 = alkyl <containing 1-6 C> / Ph
G23 = (1-3) CH2
G24 = NH2 / 56 / 58 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>

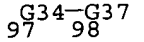


G25 = O / S / NH / 66

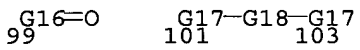


G26 = OH / alkoxy <containing 1-6 C>
G27 = CH2 / O / S / S(O) / SO2
G28 = aryl <containing up to 10 C, mono- or bicyclic> (opt. substd. by (1-4) G29) / heteroaryl <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic> (opt. substd. by (1-4) G29) / heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, mono- or bicyclic, (1) 5- or more membered ring, (1) up to 6-membered ring> (opt. substd. by (1-4) G29) / carbocycle <containing 3-10 C, non-aromatic, 0 or more double bonds, mono- or bicyclic> (opt. substd. by 1 or more G29)
G29 = alkyl <containing 1-6 C> / halo / alkyl <containing 1-6 C> (substd. by (3) halo) / OH / alkoxy <containing 1-6 C> / SH / alkylthio <containing 1-6 C> / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C>
G30 = aryl <containing up to 10 C, mono- or bicyclic> (opt. substd. by 1 or more G4)
G31 = carbocycle <containing 3-10 C, non-aromatic, 0 or more double bonds, mono- or bicyclic> (opt. substd. by 1 or more G4)
G32 = H / alkyl <containing 1-6 C> (opt. substd. by 1 or more G33) / alkenyl <containing 2-6 C> (opt. substd. by 1 or more G33) / alkynyl <containing 2-6 C> (opt. substd. by 1 or more G33) / 97 / carbocycle <containing 5-10 C, 0 or more double bonds, mono- or bicyclic, 5- or 6-membered rings only> (opt. substd. by (1-7) G41) / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, zero or more N, zero or more O,

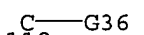
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41)



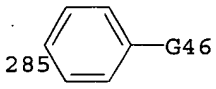
G33 = NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> /
alkyl <containing 1-6 C> (opt. substd. by (3) halo) / CN /
CO2H / alkoxycarbonyl <containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>
G34 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 99 / 101-20 103-98 /
(Specifically claimed: CH2)

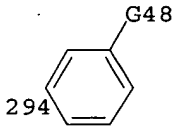


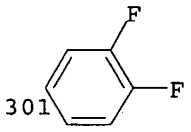
G35 = N / 118

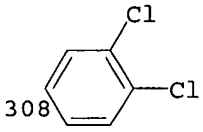


G36 = H / R
G37 = carbocycle <containing 5-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41) /
(Specifically claimed: 285 / 294 / 301 / 308)



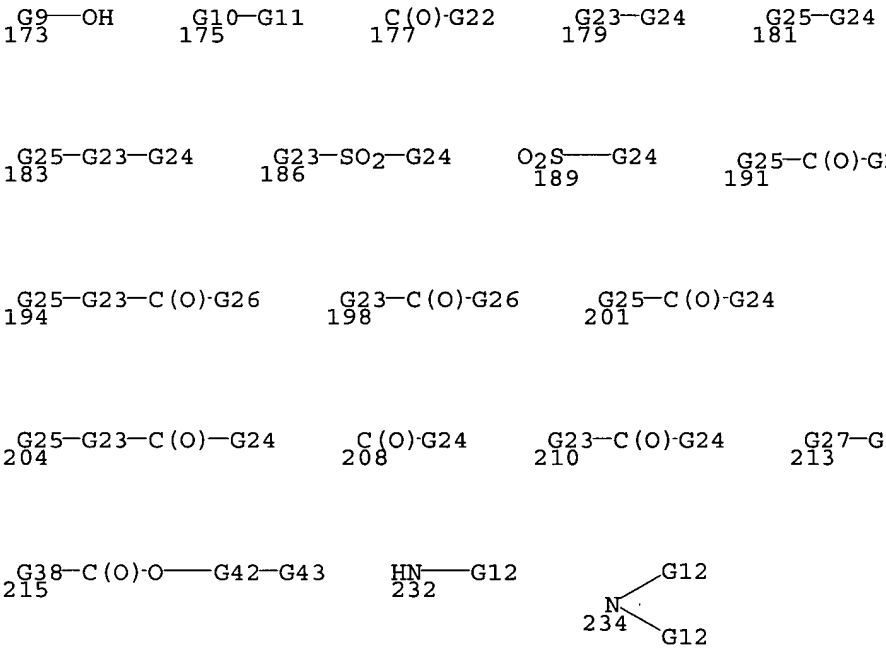






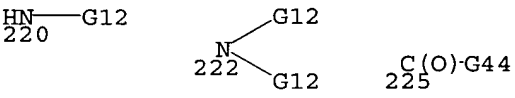
G38 = (0-3) CH2
G40 = alkyl <containing 1-6 C>
G41 = alkyl <containing 1-6 C> / halo / CN / NO2 /
alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 232 /
234 / heterocycle <containing 1-2 heteroatoms, 1 or more N,
zero or more O (no other heteroatoms),
attached through 1 or more N, 5- to 6-membered monocyclic
ring> / OH / SH / 173 / 175 / 177 / 179 / 181 / 183 / 186 /
189 / 191 / 194 / CO2H / alkoxycarbonyl <containing 1-6 C> /
198 / 201 / 204 / 208 / 210 / 213 / 215 /
aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by (1-4) G29) / heteroaryl <containing 1-4
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), mono- or bicyclic>

(opt. substd. by (1-4) G29) / heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, mono- or bicyclic, (1) 5- or more membered ring, (1) up to 6-membered ring> (opt. substd. by (1-4) G29) / carbocycle <containing 3-10 C, non-aromatic, 0 or more double bonds, mono- or bicyclic> (opt. substd. by 1 or more G29)

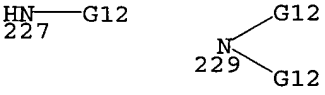


G42 = alkylene <containing 1-6 C>

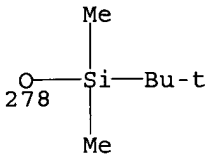
G43 = OH / alkoxy <containing 1-6 C> / NH2 / 220 / 222 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring> / 225



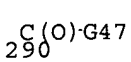
G44 = OH / alkoxy <containing 1-6 C> / NH2 / 227 / 229 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>



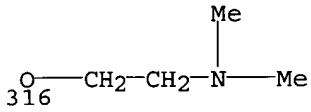
G45 = OMe / F / 278 / Ph / Cl



G46 = F / Cl / 290

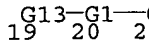


G47 = OMe / OBu-t / OH / 316 / NMe2 / piperidino / NHEt / 324

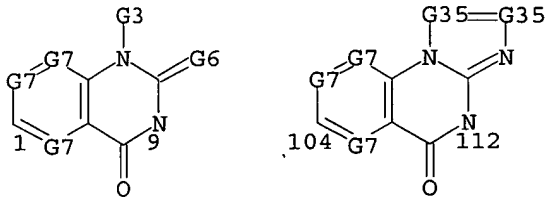


G48 = Cl / F
Patent location: claim 1
Note: and N-oxides or pharmaceutically acceptable acid or base addition salts
Note: additional heteroatom interruptions in G17 also claimed
Note: substitution is restricted
Stereochemistry: and optical isomers

MSTR 2



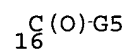
G1 = **1-19 9-21** / 104-19 112-21



G2 = alkyl <containing 1-6 C> / OH / CN
G3 = H / CF3 / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C> / alkyl <containing 1-6 C> (opt. substd. by 1 or more G4) / alkenyl <containing 2-6 C> (opt. substd. by 1 or more G4) / alkynyl <containing 2-6 C> (opt. substd. by 1 or more G4) / aryl <containing up to 10 C, mono- or bicyclic> (opt. substd. by 1 or more G4) /

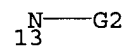
alkyl <containing 1-6 C> (substd. by 1 or more G30) /
alkyl <containing 1-6 C> (substd. by G31) /
heteroaryl <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), monocyclic> (opt. substd. by 1 or more G4) /
heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G4) / (Specifically claimed: Me)

G4 = halo / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C> / CN / alkyl <containing 1-6 C> (substd. by (3) halo) / 16 / OH / SH / alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>

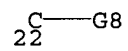


G5 = alkyl <containing 1-6 C> / Ph / OH / alkoxy <containing 1-16 C>

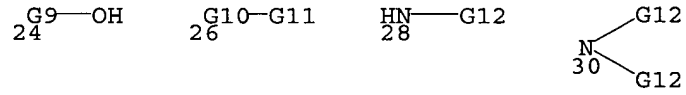
G6 = O / S / **NH** / 13



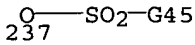
G7 = **(up to 2) N / 22**

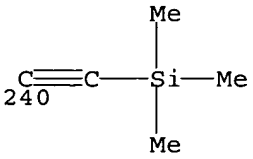


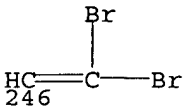
G8 = H / alkyl <containing 1-6 C> / OH / alkoxy <containing 1-6 C> / **halo** / CF3 / CN / NO2 / SH / 24 /
26 / NH2 / 28 / 30 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>



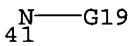
G9 = S / S(O)
G10 = S / S(O) / SO2
G11 = alkyl <containing 1-6 C>
G12 = alkyl <containing 1-6 C> / alkyl <containing 1-6 C> (substd. by 1 or more aryl <containing up to 10 C, mono- or bicyclic>)
G13 = H / halo / 237 / CHO / COMe / R <"ester group"> / 240 / ethynyl / 246



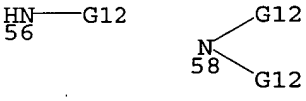




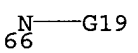
G15 = halo / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C> / OH / SH / alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C> / CO2H / alkoxycarbonyl <containing 1-6 C>
G16 = carbon chain <containing 1 or more C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)
G17 = carbon chain <containing 1 or more C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)
G18 = O / S / S(O) / SO2 / NH / 41



G19 = alkyl <containing 1-6 C>
G22 = alkyl <containing 1-6 C> / Ph
G23 = (1-3) CH2
G24 = NH2 / 56 / 58 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>



G25 = O / S / NH / 66



G26 = OH / alkoxy <containing 1-6 C>
G27 = CH2 / O / S / S(O) / SO2
G28 = aryl <containing up to 10 C, mono- or bicyclic> (opt. substd. by (1-4) G29) / heteroaryl <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic> (opt. substd. by (1-4) G29) / heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, mono- or bicyclic, (1) 5- or more membered ring, (1) up to 6-membered ring> (opt. substd. by (1-4) G29) / carbocycle <containing 3-10 C, non-aromatic, 0 or more double bonds, mono- or bicyclic> (opt. substd. by 1 or more G29)
G29 = alkyl <containing 1-6 C> / halo / alkyl <containing 1-6 C> (substd. by (3) halo) / OH /

alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C>

G30 = aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4)

G31 = carbocycle <containing 3-10 C, non-aromatic,
0 or more double bonds, mono- or bicyclic>
(opt. substd. by 1 or more G4)

G32 = H / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G33) /
alkenyl <containing 2-6 C> (opt. substd. by 1 or more G33) /
alkynyl <containing 2-6 C> (opt. substd. by 1 or more G33) /
97 / carbocycle <containing 5-10 C, 0 or more double bonds,
mono- or bicyclic, 5- or 6-membered rings only>
(opt. substd. by (1-7) G41) / heterocycle <containing 5-10
atoms, 1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41)

G34—G37
97 98

G33 = NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> /
alkyl <containing 1-6 C> (opt. substd. by (3) halo) / CN /
CO2H / alkoxycarbonyl <containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>

G34 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 99 / 101-20 103-98 /
(Specifically claimed: CH2)

G16=O G17—G18—G17
99 101 103

G35 = N / 118

C——G36
118

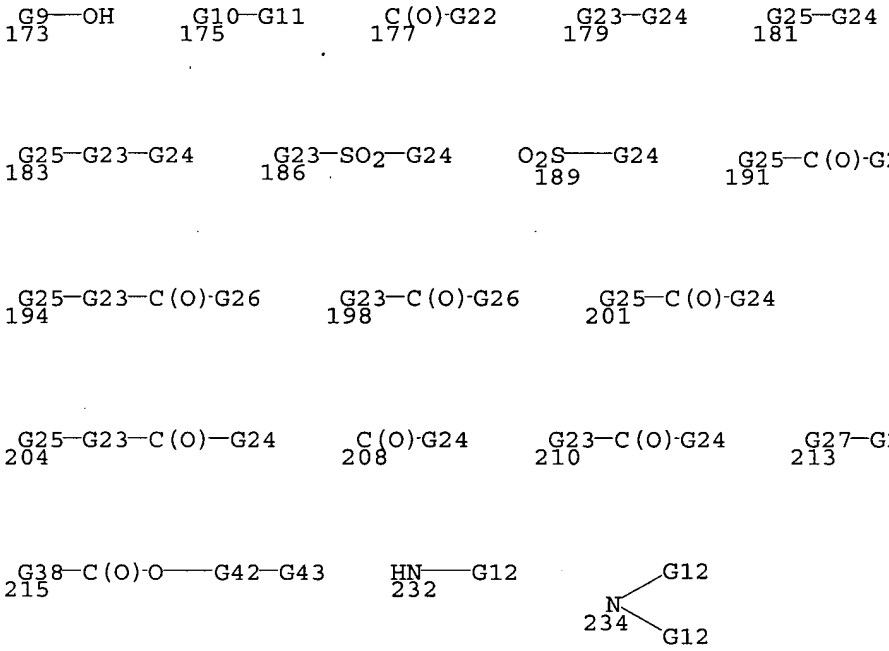
G36 = H / R

G37 = carbocycle <containing 5-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41)

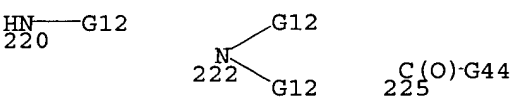
G38 = (0-3) CH2

G41 = alkyl <containing 1-6 C> / halo / CN / NO2 /
alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 232 /
234 / heterocycle <containing 1-2 heteroatoms, 1 or more N,
zero or more O (no other heteroatoms),
attached through 1 or more N, 5- to 6-membered monocyclic

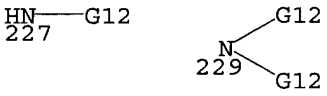
ring> / OH / SH / 173 / 175 / 177 / 179 / 181 / 183 / 186 /
189 / 191 / 194 / CO2H / alkoxycarbonyl <containing 1-6 C> /
198 / 201 / 204 / 208 / 210 / 213 / 215 /
aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by (1-4) G29) / heteroaryl <containing 1-4
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), mono- or bicyclic>
(opt. substd. by (1-4) G29) / heterocycle <containing 1-4
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), non-aromatic,
0 or more double bonds, mono- or bicyclic,
(1) 5- or more membered ring, (1) up to 6-membered ring>
(opt. substd. by (1-4) G29) / carbocycle <containing 3-10 C,
non-aromatic, 0 or more double bonds, mono- or bicyclic>
(opt. substd. by 1 or more G29)



G42 = alkylene <containing 1-6 C>
G43 = OH / alkoxy <containing 1-6 C> / NH2 / 220 / 222 /
heterocycle <containing 1-2 heteroatoms, 1 or more N,
zero or more O (no other heteroatoms),
attached through 1 or more N, 5- to 6-membered monocyclic
ring> / 225



G44 = OH / alkoxy <containing 1-6 C> / NH2 / 227 / 229 /
heterocycle <containing 1-2 heteroatoms, 1 or more N,
zero or more O (no other heteroatoms),
attached through 1 or more N, 5- to 6-membered monocyclic
ring>

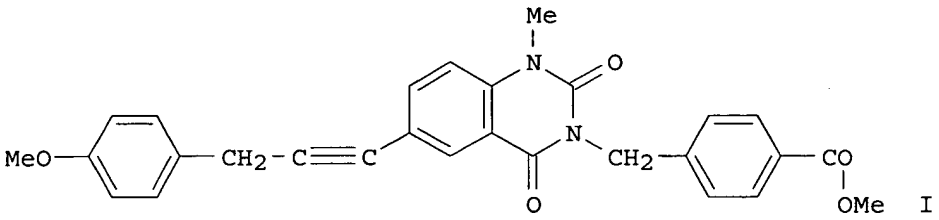


G45 = Me / CF3
Patent location: claim 12
Note: additional heteroatom interruptions in G17 also claimed
Note: substitution is restricted

L86 ANSWER 10 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:105274 MARPAT
TITLE: Combination of an allosteric alkyne inhibitor of matrix metalloproteinase-13 with a selective inhibitor of cyclooxygenase-2
INVENTOR(S): Roark, William Howard
PATENT ASSIGNEE(S): Warner-Lambert Company Llc, USA
SOURCE: PCT Int. Appl., 196 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007025	A1	20040122	WO 2003-IB3043	20030707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2491820	AA	20040122	CA 2003-2491820	20030707
AU 2003281168	A1	20040202	AU 2003-281168	20030707
EP 1525030	A1	20050427	EP 2003-740952	20030707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012666	A	20050510	BR 2003-12666	20030707
JP 2006502991	T2	20060126	JP 2004-520997	20030707
US 2004019055	A1	20040129	US 2003-620173	20030715
PRIORITY APPLN. INFO.:			US 2002-396385P	20020717
			WO 2003-IB3043	20030707

GI

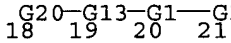


I

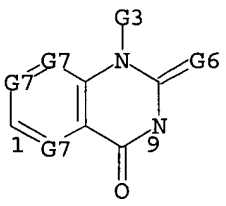
AB The invention provides a combination, comprising an allosteric alkyne inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with a selective inhibitor of COX-2, or a pharmaceutically acceptable salt thereof, that is not celecoxib or valdecoxib. This invention also provides a combination comprising an NSAID, or a pharmaceutically acceptable salt thereof, and an allosteric alkyne inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof. This invention also provides a method of treating a disease that is responsive to inhibition of MMP-13 and cyclooxygenase 1 or cyclooxygenase-2, comprising administering to a patient suffering from such a disease the invention combination comprising an allosteric alkyne inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with an NSAID, or a pharmaceutically acceptable salt thereof. Biol. examples include methods to determine inhibition of MMP-13 and COX-2 by the compds. and chemical-induced arthritis in animals. Pharmaceutical formulations are also given. An example MMP-13 inhibitor is I.

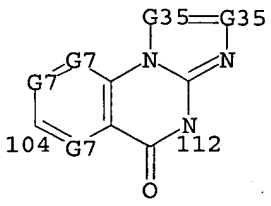
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1



G1 = **1-19 9-21** / 104-19 112-21

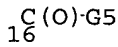




G2 = alkyl <containing 1-6 C> / OH / CN
G3 = H / CF3 / NH2 / alkylamino <containing 1-10 C> /
dialkylamino <each alkyl containing 1-10 C> /
alkyl <containing 1-6 C> (opt. substd. by 1 or more G4) /
alkenyl <containing 2-6 C> (opt. substd. by 1 or more G4) /
alkynyl <containing 2-6 C> (opt. substd. by 1 or more G4) /
aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4) /
alkyl <containing 1-10 C> (substd. by 1 or more G30) /
alkyl <containing 1-10 C> (substd. by G31) /
heteroaryl <containing 1-4 heteroatoms, zero or more N,

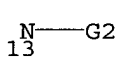
zero or more O, zero or more S (no other heteroatoms), monocyclic> (opt. substd. by 1 or more G4) / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G4) / (Specifically claimed: Me)

G4 = halo / NH2 / alkylamino <containing 1-10 C> / dialkylamino <each alkyl containing 1-10 C> / CN / alkyl <containing 1-6 C> (substd. by (3) halo) / 16 / OH / SH / alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>



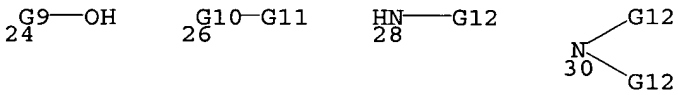
G5 = alkyl <containing 1-6 C> / Ph / OH / alkoxy <containing 1-16 C>

G6 = O / S / **NH** / 13



G7 = **(up to 2) N / 22**

G8 = H / alkyl <containing 1-6 C> / OH / alkoxy <containing 1-6 C> / **halo** / CF3 / CN / NO2 / SH / 24 / 26 / NH2 / 28 / 30 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring> (opt. substd. by alkyl <containing 1-10 C>)



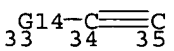
G9 = S / S(O)

G10 = S / S(O) / SO2

G11 = alkyl <containing 1-6 C>

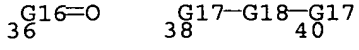
G12 = alkyl <containing 1-6 C> / alkyl <containing 1-6 C> (substd. by 1 or more aryl <containing up to 10 C, mono- or bicyclic>)

G13 = ethynylene / 33-18 35-20

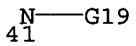


G14 = carbon chain <containing 1 or more C, up to 2 double bonds, up to 2 triple bonds> (opt. substd. by 1 or more G15) / 36 / 38-18 40-34 /

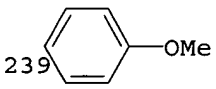
(Specifically claimed: CH2)



G15 = halo / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C> / OH / SH / alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C> / CO2H / alkoxycarbonyl <containing 1-6 C>
G16 = carbon chain <containing 1 or more C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)
G17 = carbon chain <containing 1 or more C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)
G18 = O / S / S(O) / SO2 / NH / 41

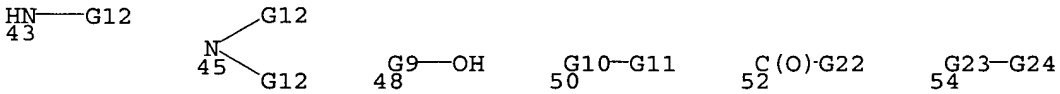


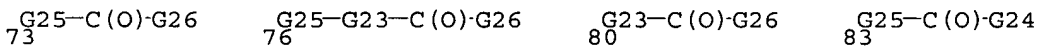
G19 = alkyl <containing 1-6 C>
G20 = aryl <containing up to 10 C, mono- or bicyclic> (opt. substd. by (1-7) G21) / heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by (1-7) G21) / carbocycle <containing 5-6 C, non-aromatic, 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by (1-7) G21) / carbocycle <containing 8-10 C, 0 or more double bonds, mono- or bicyclic, 5- or 6-membered rings only> (opt. substd. by (1-7) G21) / heterocycle <containing 8-10 atoms, 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 5- or 6-membered rings only> (opt. substd. by (1-7) G21) / (Specifically claimed: 239 / Ph)

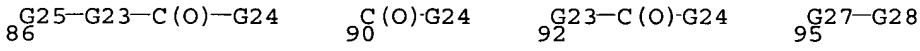


G21 = alkyl <containing 1-10 C> / halo / CN / NO2 / alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 43 / 45 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring> / OH / SH / 48 / 50 / 52 / 54 / 61 / 63 / 68 / 71 / 73 / 76 / CO2H / alkoxycarbonyl <containing 1-6 C> / 80 / 83 / 86 / 90 / 92 / 95 / carbocycle <containing 6 C, aromatic, 6 normalized bonds, 6-membered monocyclic ring> (opt. substd. by (1-3) G29) / heteroaryl <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), monocyclic> (opt. substd. by (1-3) G29) / cycloalkyl <containing 5-6 C> (opt. substd. by (1-3) G29) / heterocycle <containing 1-3

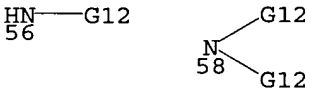
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), non-aromatic,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by (1-3) G29)



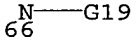




G22 = alkyl <containing 1-6 C> / Ph
G23 = (1-3) CH2
G24 = NH2 / 56 / 58 / heterocycle <containing 1-2
heteroatoms, 1 or more N, zero or more O (no other
heteroatoms), attached through 1 or more N,
5- to 6-membered monocyclic ring>



G25 = O / S / NH / 66



G26 = OH / alkoxy <containing 1-6 C>
G27 = CH2 / O / S / S(O) / SO2
G28 = carbocycle <containing 6 C, aromatic,
6 normalized bonds, 6-membered monocyclic ring>
(opt. substd. by (1-3) G29) / heteroaryl <containing 1-4
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), monocyclic>
(opt. substd. by (1-3) G29) / cycloalkyl <containing 5-6 C>
(opt. substd. by (1-3) G29) / heterocycle <containing 1-3
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), non-aromatic,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by (1-3) G29)
G29 = alkyl <containing 1-10 C> / halo /
alkyl <containing 1-6 C> (substd. by (3) halo) / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / NH2 /

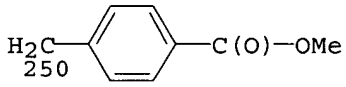
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C>

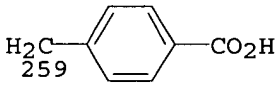
G30 = aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4)

G31 = cycloalkyl <containing 3-10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4)

G32 = H / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G33) /
alkenyl <containing 2-6 C> (opt. substd. by 1 or more G33) /
alkynyl <containing 2-6 C> (opt. substd. by 1 or more G33) /
97 / carbocycle <containing 5-10 C, 0 or more double bonds,
mono- or bicyclic, 5- or 6-membered rings only>
(opt. substd. by (1-7) G41) / heterocycle <containing 5-10
atoms, 1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41) /
(Specifically claimed: 250 / 259 / CH2Ph)

G34—G37
97 98





G33 = NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> /
alkyl <containing 1-6 C> (opt. substd. by (3) halo) / CN /
CO2H / alkoxycarbonyl <containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>

G34 = carbon chain <containing 1 or more C,
up to 2 double bonds, up to 2 triple bonds>
(opt. substd. by 1 or more G15) / 99 / 101-20 103-98

G16=O G17—G18—G17
99 101 103

G35 = N / 118

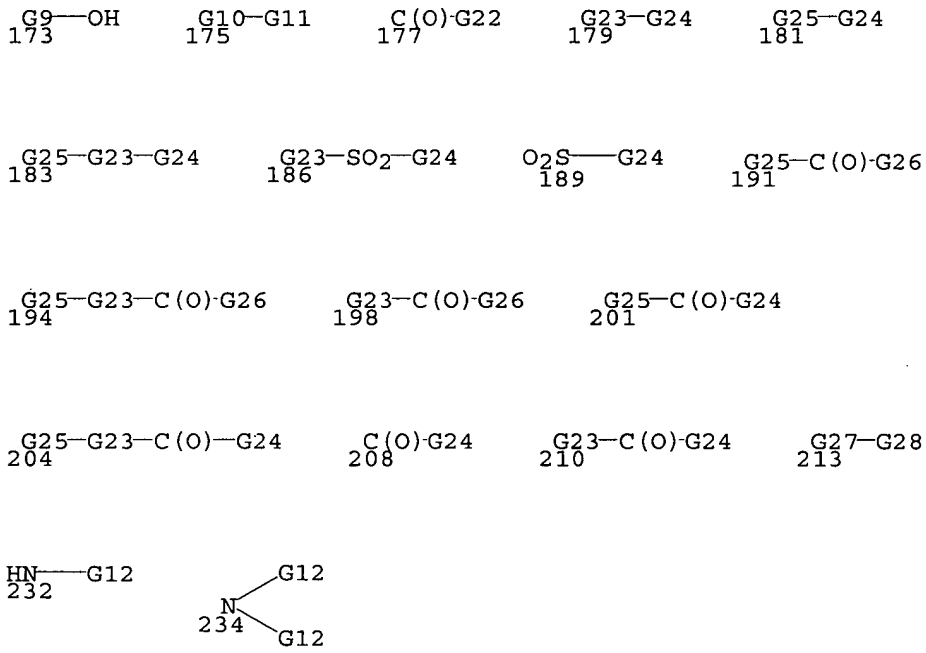
C——G36
118

G36 = H / R

G37 = carbocycle <containing 5-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41)

G41 = alkyl <containing 1-6 C> / halo / CN / NO2 /
alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 232 /
234 / heterocycle <containing 1-2 heteroatoms, 1 or more N,
zero or more O (no other heteroatoms),
attached through 1 or more N, 5- to 6-membered monocyclic
ring> / OH / SH / 173 / 175 / 177 / 179 / 181 / 183 / 186 /
189 / 191 / 194 / CO2H / alkoxycarbonyl <containing 1-6 C> /
198 / 201 / 204 / 208 / 210 / 213 /

carbocycle <containing 6 C, aromatic, 6 normalized bonds,
6-membered monocyclic ring> (opt. substd. by (1-3) G29) /
heteroaryl <containing 1-4 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
monocyclic> (opt. substd. by (1-3) G29) /
cycloalkyl <containing 5-6 C> (opt. substd. by (1-3) G29) /
heterocycle <containing 1-3 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
non-aromatic, 0 or more double bonds,
5- to 6-membered monocyclic ring>
(opt. substd. by (1-3) G29)



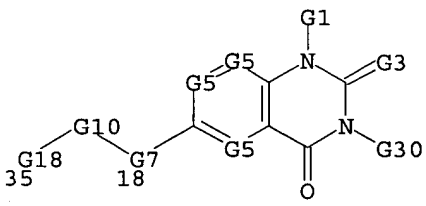
Patent location: claim 1
Note: or pharmaceutically acceptable salts or N-oxides
Note: additional heteroatom interruptions in G17 also claimed
Note: substitution is restricted
Note: additional ring formation also claimed

L86 ANSWER 11 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:105336 MARPAT
TITLE: Combination of an allosteric carboxylic inhibitor of matrix metalloproteinase-13 with a selective inhibitor of cyclooxygenase-2 that is not celecoxib or valdecoxib, and therapeutic use
INVENTOR(S): Roark, William Howard
PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA
SOURCE: PCT Int. Appl., 239 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006931	A2	20040122	WO 2003-IB3098	20030707
WO 2004006931	A3	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2492387	AA	20040122	CA 2003-2492387	20030707
AU 2003281170	A1	20040202	AU 2003-281170	20030707
BR 2003012744	A	20050426	BR 2003-12744	20030707
EP 1530475	A2	20050518	EP 2003-740981	20030707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006503812	T2	20060202	JP 2004-521004	20030707
US 2004019054	A1	20040129	US 2003-619769	20030715
PRIORITY APPLN. INFO.:			US 2002-396785P	20020717
			WO 2003-IB3098	20030707

AB The invention provides a combination comprising an allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with a selective inhibitor of COX-2, or a pharmaceutically acceptable salt thereof, that is not celecoxib or valdecoxib, and their use for the treatment of diseases that are responsive to inhibition of MMP-13 and cyclooxygenase-2.

MSTR 1



G1 = H / NH2 / alkyl <containing 1-6 C> (opt. substd.) / alkenyl <containing 3-6 C> (opt. substd.) / alkynyl <containing 3-6 C> (opt. substd.) / alkyl <containing 1-6 C> (substd. by alkylamino <containing 1-6 C> (opt. substd.)) / alkyl <containing 1-6 C> (substd. by dialkylamino <each alkyl containing 1-6 C> (opt. substd.)) / aryl <containing up to 10 C, mono- or bicyclic> (opt. substd.) / alkyl <containing 1-6 C> (substd. by 1 or more G2) / heterocycle <containing 5-6 atoms, 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd.) / alkyl <containing 1-6 C> (substd. by cycloalkyl <containing 3-6 C> (opt. substd.)) / (Specifically claimed: Me)

G2 = aryl <containing up to 10 C, mono- or bicyclic>

(opt. substd.)
G3 = O / S / **14**

N—G4
14

G4 = alkyl <containing 1-6 C> (opt. substd.) / OH / CN
G5 = **(up to 2) N / 16**

C—G6
16

G6 = H / alkyl <containing 1-6 C> (opt. substd.) / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / OH /
alkoxy <containing 1-6 C> (opt. substd.) / **F** / Cl / Br / I
G7 = **bond** / 26

C═G8
26

G8 = O / S / NH / 20

N—G9
20

G9 = alkyl <containing 1-6 C> (opt. substd.)
G10 = 24-35 25-18 / carbon chain <containing 1 or more
C, 0 or more double bonds> (opt. substd. by 1 or more G14)

G11—G12
24 25

G11 = carbon chain <containing 1 or more C,
0 or more double bonds> (opt. substd. by 1 or more G14) /
(Specifically claimed: CH2)
G12 = O / S / NH / 28

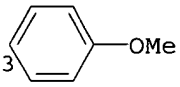
N—G13
28

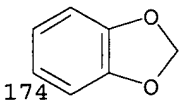
G13 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G2) /
aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd.) / cycloalkyl / heteroaryl <containing zero or
more N, zero or more O, zero or more S (no other heteroatoms)
> (opt. substd.)
G14 = F / Cl / Br / I / NH2 / OH / SH / 30 / 32 /
aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd.) / heterocycle <containing zero or more N,
zero or more O, zero or more S, 0 or more double bonds>
(opt. substd.) / cycloalkyl

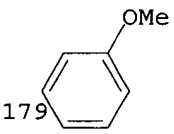
30 G15—G16

32 C(O)-G17

G15 = O / S
G16 = alkyl <containing 1-6 C> (opt. substd.)
G17 = OH / alkoxy <containing 1-6 C> (opt. substd.)
G18 = carbocycle <containing 5-6 C,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by (1-7) G19) / heterocycle <containing 5-6
atoms, 1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by (1-7) G19) / carbocycle <containing 8-10 C,
0 or more double bonds, bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G19) /
heterocycle <containing 8-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G19) /
(Specifically claimed: 163 / 174 / 179)

163 

174 

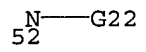
179 

G19 = alkyl <containing 1-6 C> (opt. substd.) / F / Cl /
Br / I / CN / NO2 / SCF3 / CF3 / OCF3 / NH2 /
alkylamino <containing 1-6 C> (opt. substd.) /
dialkylamino <each alkyl containing 1-6 C> (opt. substd.) /
OH / SH / 36 / 38 / 40 / 42 / 45 / 48 / 54 / 56 / 59

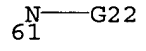
36 G20—OH 38 G21—G22 40 O_2S—G23 42 G24—SO_2—G23 45 G25—C(O)-G26

48 G25—G24—C(O)-G26 54 C(O)-G26 56 G24—C(O)-G26 59 G27—G28

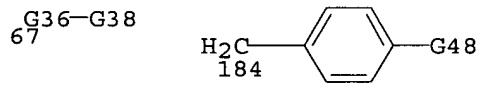
G20 = S / S(O)
G21 = O / S / S(O) / SO2
G22 = alkyl <containing 1-6 C> (opt. substd.)
G23 = NH2 / alkylamino <containing 1-6 C> (opt. substd.) /
dialkylamino <each alkyl containing 1-6 C> (opt. substd.)
G24 = (1-3) CH2
G25 = O / S / S(O) / SO2 / NH / 52



G26 = OH / alkoxy <containing 1-6 C> (opt. substd.) /
NH2 / alkylamino <containing 1-6 C> (opt. substd.) /
dialkylamino <each alkyl containing 1-6 C> (opt. substd.)
G27 = CH2 / O / S / S(O) / SO2 / NH / 61



G28 = carbocycle <containing 5-6 C,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G29) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G29)
G29 = alkyl <containing 1-6 C> (opt. substd.) / F / Cl /
Br / I / OH / NH2
G30 = H / carbon chain <containing 1-6 C>
(opt. substd. by 1 or more G31) / 67 /
carbocycle <containing 5-6 C, 0 or more double bonds,
5- to 6-membered monocyclic ring>
(opt. substd. by (1-7) G39) / heterocycle <containing 5-6
atoms, 1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by (1-7) G39) / carbocycle <containing 8-10 C,
0 or more double bonds, bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G39) /
heterocycle <containing 8-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G39) /
(Specifically claimed: 184)

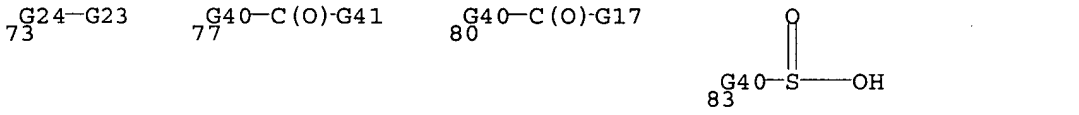


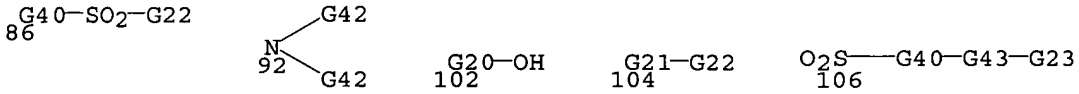
G31 = NH2 / CN / alkyl <containing 1-6 C>
(substd. by 1 or more G32) / cycloalkyl / 63 / OH / SH / 65

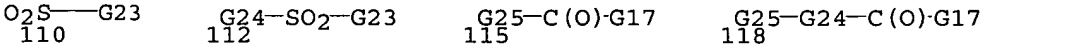
G32 = F / Cl / Br / I
G33 = NH2 / alkylamino <containing 1-6 C> (opt. substd.) /
dialkylamino <each alkyl containing 1-6 C> (opt. substd.) /
OH / alkoxy <containing 1-6 C> (opt. substd.)
G34 = O / S
G35 = alkyl <containing 1-6 C> (opt. substd.)

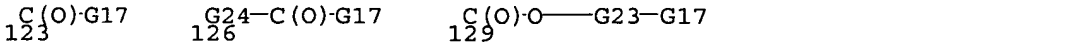
G36 = carbon chain <containing 1 or more C,
0 or more double bonds> (opt. substd. by 1 or more G37)
G37 = Ph / F / Cl / Br / I / NH2 / OH / SH / 69 / 71

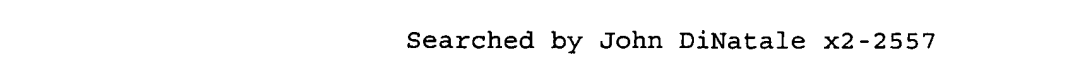
G38 = carbocycle <containing 5-6 C,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by (1-7) G39) / heterocycle <containing 5-6
atoms, 1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by (1-7) G39) / carbocycle <containing 8-10 C,
0 or more double bonds, bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G39) /
heterocycle <containing 8-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G39)
G39 = alkyl <containing 1-6 C> (opt. substd.) / F / Cl /
Br / I / CN / NO2 / CF3 / OCF3 /
alkylamino <containing 1-6 C> (opt. substd.) /
dialkylamino <each alkyl containing 1-6 C> (opt. substd.) /
73 / 77 / 80 / 83 / 86 / 92 / OH / SH / 102 / 104 / 106 /
110 / 112 / 115 / 118 / 123 / 126 / 129 / 133 / 138 / 141 /
146 / 149 / 152 / 155 / carbocycle <containing 5-6 C,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd.) / heterocycle <containing 5-6 atoms,
1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd.) / 157

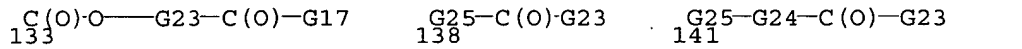




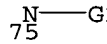




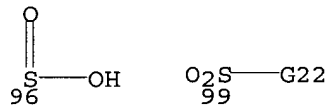




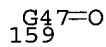
G40 = NH / 75



G41 = H / alkyl <containing 1-6 C> (opt. substd.)
G42 = 96 / 99



G43 = (1-4) CH2
G44 = cycloalkylene <containing 3-6 C>
G45 = carbocycle <containing 5-6 C,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd.) / heterocycle <containing 5-6 atoms,
1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd.) / 159



G47 = carbocycle <containing 5-6 C,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd.) / heterocycle <containing 5-6 atoms,
1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd.)
G48 = CO2H / H / CO2Me / CN
Patent location: claim 1
Note: or pharmaceutically acceptable salts or N-oxides
Note: substitution is restricted

L86 ANSWER 12 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:105335 MARPAT
TITLE: Combination of an allosteric alkyne inhibitor of matrix metalloproteinase-13 with celecoxib or valdecoxib, pharmaceutical compositions, and therapeutic use
INVENTOR(S): Roark, William Howard
PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA

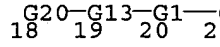
SOURCE: PCT Int. Appl., 188 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006914	A1	20040122	WO 2003-IB3154	20030707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2489722	AA	20040122	CA 2003-2489722	20030707
AU 2003249505	A1	20040202	AU 2003-249505	20030707
BR 2003012708	A	20050426	BR 2003-12708	20030707
EP 1534274	A1	20050601	EP 2003-764068	20030707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006502114	T2	20060119	JP 2004-521017	20030707
US 2004023969	A1	20040205	US 2003-619777	20030715
PRIORITY APPLN. INFO.:			US 2002-396922P	20020717
			WO 2003-IB3154	20030707

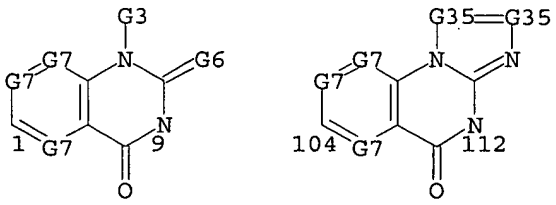
AB The invention provides a combination comprising an allosteric alkyne inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a pharmaceutically acceptable salt thereof. This invention also provides a method of treating a disease that is responsive to inhibition of MMP-13 and cyclooxygenase-2, comprising administering to a patient suffering from such a disease the invention combination comprising an allosteric alkyne inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a pharmaceutically acceptable salt thereof. This invention also provides a pharmaceutical composition, comprising the invention combination comprising an allosteric alkyne inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, or excipient. The invention combinations may also be further combined with other pharmaceutical agents depending on the disease being treated.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1



G1 = **1-19 9-21** / 104-19 112-21



G2 = alkyl <containing 1-6 C> / OH / CN
G3 = H / CF3 / NH2 / alkylamino <containing 1-10 C> /
dialkylamino <each alkyl containing 1-10 C> /
alkyl <containing 1-6 C> (opt. substd. by 1 or more G4) /
alkenyl <containing 2-6 C> (opt. substd. by 1 or more G4) /
alkynyl <containing 2-6 C> (opt. substd. by 1 or more G4) /
aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4) /
alkyl <containing 1-10 C> (substd. by 1 or more G30) /
alkyl <containing 1-10 C> (substd. by G31) /
heteroaryl <containing 1-4 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
monocyclic> (opt. substd. by 1 or more G4) /
heterocycle <containing 1-3 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
non-aromatic, 0 or more double bonds,
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G4) / (Specifically claimed: Me)
G4 = halo / NH2 / alkylamino <containing 1-10 C> /
dialkylamino <each alkyl containing 1-10 C> / CN /
alkyl <containing 1-6 C> (substd. by (3) halo) / 16 / OH /
SH / alkoxy <containing 1-6 C> /
alkylthio <containing 1-6 C>

C(O)-G5
16

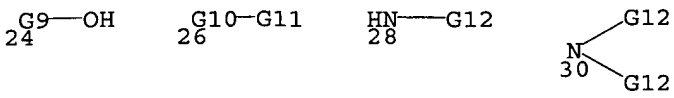
G5 = alkyl <containing 1-6 C> / Ph / OH /
alkoxy <containing 1-16 C>
G6 = O / S / **NH** / 13

N——G2
13

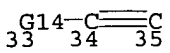
G7 = **(up to 2) N / 22**

C——G8
22

G8 = H / alkyl <containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / **halo** / CF3 / CN / NO2 / SH / 24
/
26 / NH2 / 28 / 30 / heterocycle <containing 1-2
heteroatoms, 1 or more N, zero or more O (no other
heteroatoms), attached through 1 or more N,
5- to 6-membered monocyclic ring>
(opt. substd. by alkyl <containing 1-10 C>)

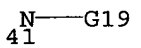


G9 = S / S(O)
G10 = S / S(O) / SO2
G11 = alkyl <containing 1-6 C>
G12 = alkyl <containing 1-6 C> /
alkyl <containing 1-6 C> (substd. by 1 or more aryl
<containing up to 10 C, mono- or bicyclic>)
G13 = ethynylene / 33-18 35-20

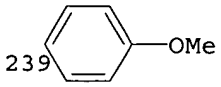


G14 = carbon chain <containing 1 or more C,
up to 2 double bonds, up to 2 triple bonds>
(opt. substd. by 1 or more G15) / 36 / 38-18 40-34 /
(Specifically claimed: CH2)

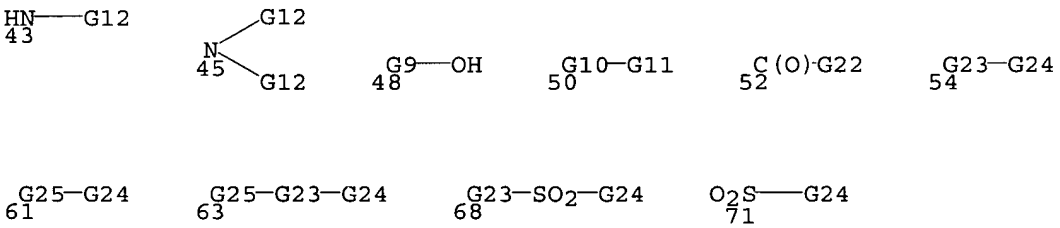
G15 = halo / NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C> /
CO2H / alkoxycarbonyl <containing 1-6 C>
G16 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G17 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G18 = O / S / S(O) / SO2 / NH / 41



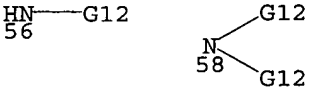
G19 = alkyl <containing 1-6 C>
G20 = aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by (1-7) G21) / heterocycle <containing 1-4
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by (1-7) G21) / carbocycle <containing 5-6 C,
non-aromatic, 0 or more double bonds,
5- to 6-membered monocyclic ring>
(opt. substd. by (1-7) G21) / carbocycle <containing 8-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
heterocycle <containing 8-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
(Specifically claimed: 239 / Ph)



G21 = alkyl <containing 1-10 C> / halo / CN / NO2 / alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 43 / 45 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring> / OH / SH / 48 / 50 / 52 / 54 / 61 / 63 / 68 / 71 / 73 / 76 / CO2H / alkoxycarbonyl <containing 1-6 C> / 80 / 83 / 86 / 90 / 92 / 95 / carbocycle <containing 6 C, aromatic, 6 normalized bonds, 6-membered monocyclic ring> (opt. substd. by (1-3) G29) / heteroaryl <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), monocyclic> (opt. substd. by (1-3) G29) / cycloalkyl <containing 5-6 C> (opt. substd. by (1-3) G29) / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by (1-3) G29)



G22 = alkyl <containing 1-6 C> / Ph
G23 = (1-3) CH2
G24 = NH2 / 56 / 58 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>

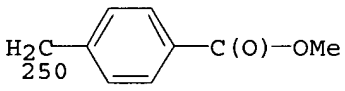


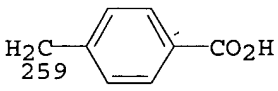
G25 = O / S / NH / 66

N—G19
66

G26 = OH / alkoxy <containing 1-6 C>
G27 = CH2 / O / S / S(O) / SO2
G28 = carbocycle <containing 6 C, aromatic,
6 normalized bonds, 6-membered monocyclic ring>
(opt. substd. by (1-3) G29) / heteroaryl <containing 1-4
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), monocyclic>
(opt. substd. by (1-3) G29) / cycloalkyl <containing 5-6 C>
(opt. substd. by (1-3) G29) / heterocycle <containing 1-3
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), non-aromatic,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by (1-3) G29)
G29 = alkyl <containing 1-10 C> / halo /
alkyl <containing 1-6 C> (substd. by (3) halo) / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C>
G30 = aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4)
G31 = cycloalkyl <containing 3-10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4)
G32 = H / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G33) /
alkenyl <containing 2-6 C> (opt. substd. by 1 or more G33) /
alkynyl <containing 2-6 C> (opt. substd. by 1 or more G33) /
97 / carbocycle <containing 5-10 C, 0 or more double bonds,
mono- or bicyclic, 5- or 6-membered rings only>
(opt. substd. by (1-7) G41) / heterocycle <containing 5-10
atoms, 1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41) /
(Specifically claimed: 250 / 259 / CH2Ph)

G34—G37
97 98

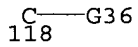




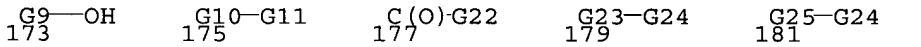
G33 = NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> /
alkyl <containing 1-6 C> (opt. substd. by (3) halo) / CN /
CO2H / alkoxycarbonyl <containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>
G34 = carbon chain <containing 1 or more C,
up to 2 double bonds, up to 2 triple bonds>
(opt. substd. by 1 or more G15) / 99 / 101-20 103-98

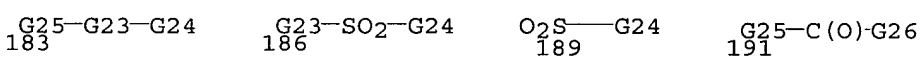
G16=O G17—G18—G17
99 101 103

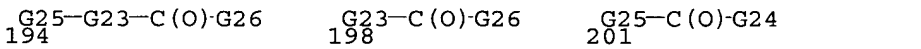
G35 = N / 118

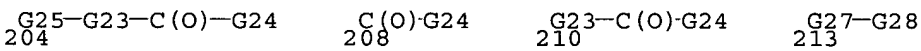


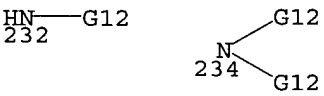
G36 = H / R
G37 = carbocycle <containing 5-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41)
G41 = alkyl <containing 1-6 C> / halo / CN / NO2 /
alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 232 /
234 / heterocycle <containing 1-2 heteroatoms, 1 or more N,
zero or more O (no other heteroatoms),
attached through 1 or more N, 5- to 6-membered monocyclic
ring> / OH / SH / 173 / 175 / 177 / 179 / 181 / 183 / 186 /
189 / 191 / 194 / CO2H / alkoxycarbonyl <containing 1-6 C> /
198 / 201 / 204 / 208 / 210 / 213 /
carbocycle <containing 6 C, aromatic, 6 normalized bonds,
6-membered monocyclic ring> (opt. substd. by (1-3) G29) /
heteroaryl <containing 1-4 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
monocyclic> (opt. substd. by (1-3) G29) /
cycloalkyl <containing 5-6 C> (opt. substd. by (1-3) G29) /
heterocycle <containing 1-3 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
non-aromatic, 0 or more double bonds,
5- to 6-membered monocyclic ring>
(opt. substd. by (1-3) G29)











Patent location: claim 1

Note: or pharmaceutically acceptable salts or N-oxides
Note: additional heteroatom interruptions in G17 also claimed
Note: substitution is restricted
Note: additional ring formation also claimed

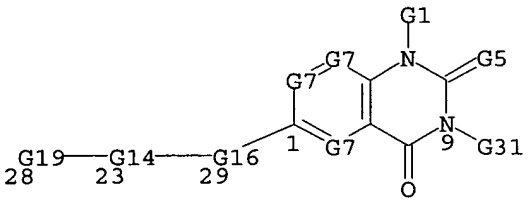
L86 ANSWER 13 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:105333 MARPAT
TITLE: Combination of an allosteric carboxylic inhibitor of matrix metalloproteinase-13 with celecoxib or valdecoxib, pharmaceutical compositions, and therapeutic use
INVENTOR(S): Roark, William Howard
PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA
SOURCE: PCT Int. Appl., 238 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006912	A2	20040122	WO 2003-IB3044	20030707
WO 2004006912	A3	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2495432	AA	20040122	CA 2003-2495432	20030707
AU 2003281169	A1	20040202	AU 2003-281169	20030707
BR 2003012736	A	20050426	BR 2003-12736	20030707
EP 1530467	A2	20050518	EP 2003-740953	20030707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006503811	T2	20060202	JP 2004-520998	20030707
US 2004019053	A1	20040129	US 2003-619662	20030715
PRIORITY APPLN. INFO.:			US 2002-396903P	20020717
			WO 2003-IB3044	20030707

AB The invention provides a combination comprising an allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a pharmaceutically acceptable salt thereof. The invention also provides a method of treating a disease that is responsive to inhibition of MMP-13 and cyclooxygenase 2, comprising administering to a patient suffering from such a disease the invention combination comprising an allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a pharmaceutically acceptable salt thereof. The invention also provides a pharmaceutical composition, comprising the invention combination comprising an allosteric carboxylic inhibitor of MMP-13, or a pharmaceutically acceptable salt thereof, with celecoxib, or a pharmaceutically acceptable salt thereof, or valdecoxib, or a

pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, or excipient. The invention combination may also be further combined with other pharmaceutical agents depending on the disease being treated.

MSTR 1



G1 = H / NH2 / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G2) /
alkenyl <containing 3-6 C> (opt. substd. by 1 or more G3) /
alkynyl <containing 3-6 C> (opt. substd. by 1 or more G3) /
aryl (opt. substd. by 1 or more G3) /
heterocycle <containing zero or more N, zero or more O, zero or more S> (opt. substd. by 1 or more G3) /
(Specifically claimed: Me)

G2 = alkylamino <containing 1-6 C>
(opt. substd. by 1 or more G3) /
dialkylamino <each alkyl containing 1-6 C>
(opt. substd. by 1 or more G3) /
aryl (opt. substd. by 1 or more G3) /
cycloalkyl <containing 3-6 C> (opt. substd. by 1 or more G3) / NH2 / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G4) / CN / CO2H /
alkoxycarbonyl <containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C>

G3 = NH2 / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G4) / CN / CO2H /
alkoxycarbonyl <containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C>

G4 = F / Cl / Br / I

G5 = O / S / **16**

N—G6
16

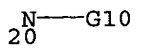
G6 = alkyl <containing 1-6 C> / OH / CN

G7 = **(up to 2) N / 18**

C—G8
18

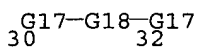
G8 = H / alkyl <containing 1-6 C> / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / **F** / Cl / Br / I

G9 = O / S / NH / 20

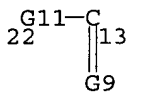


G10 = alkyl <containing 1-6 C>
G11 = O / S / NH / 24 / 26

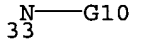
G12 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more aryl) / cycloalkyl / aryl /
heteroaryl <containing zero or more N, zero or more O,
zero or more S>
G13 = H / alkyl <containing 1-6 C>
(opt. substd. by 1 or more aryl) / aryl /
heterocycle <containing zero or more N, zero or more O,
zero or more S> / cycloalkyl
G14 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 30-28 32-29 /
(Specifically claimed: CH2)



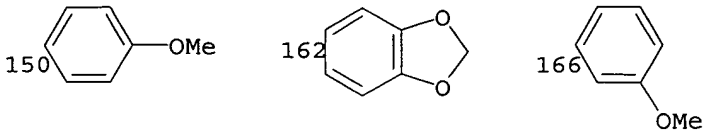
G15 = F / Cl / Br / I / NH2 / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / CO2H /
alkoxycarbonyl <containing 1-6 C>
G16 = 22-23 13-1 / **bond**



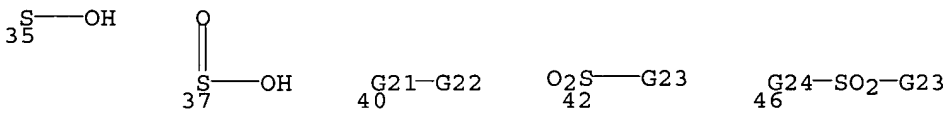
G17 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G18 = O / S / S(O) / SO2 / NH / 33

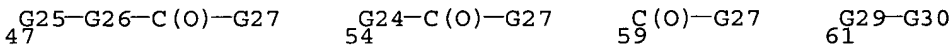


G19 = carbocycle <containing 5-10 C, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G20) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms), mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G20) /
(Specifically claimed: 150 / 162 / 166)

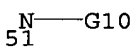


G20 = alkyl <containing 1-6 C> / F / Cl / Br / I / CN /
NO2 / SCF3 / CF3 / OCF3 / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / OH / SH / 35 /
37 / 40 / 42 / 46 / 47 / 54 / 59 /
carbocycle <containing 5-6 C, 5- to 6-membered monocyclic
ring> (opt. substd. by 1 or more G28) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G28) / 61

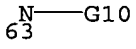




G21 = O / S / S(O) / SO2
G22 = alkyl <containing 1-6 C>
G23 = NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C>
G24 = (1-3) CH2
G25 = O / S / S(O) / SO2 / NH / 51



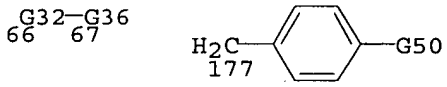
G26 = (0-3) CH2
G27 = OH / alkoxy <containing 1-6 C> / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C>
G28 = alkyl <containing 1-6 C> / F / Cl / Br / I / OH /
NH2
G29 = CH2 / O / S / S(O) / SO2 / NH / 63



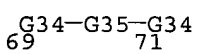
G30 = carbocycle <containing 5-6 C,
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G28) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,

zero or more S (no other heteroatoms),
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G28)

G31 = H / alkyl <containing 1 or more C> (opt. substd.) /
alkenyl <containing 3 or more C> (opt. substd.) /
alkynyl <containing 3 or more C> (opt. substd.) / 66 /
carbocycle <containing 5-10 C, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G37) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms), mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G37) /
(Specifically claimed: 177)



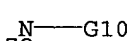
G32 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G33) / 69-9 71-67 /
(Specifically claimed: CH2)



G33 = Ph / F / Cl / Br / I / NH2 / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / CO2H /
alkoxycarbonyl <containing 1-6 C>

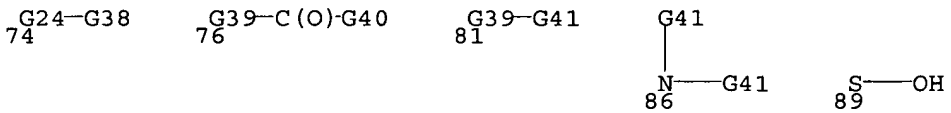
G34 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)

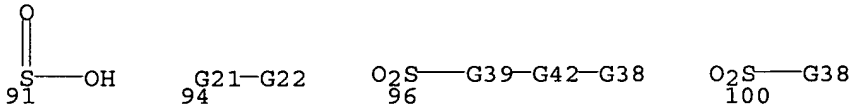
G35 = O / S / S(O) / SO2 / NH / 72 / C(O)

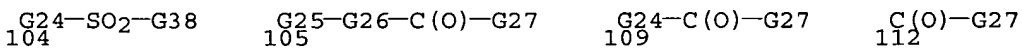


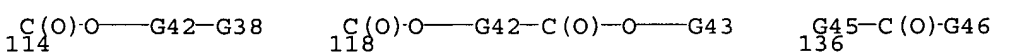
G36 = carbocycle <containing 5-10 C, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G37) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms), mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G37)

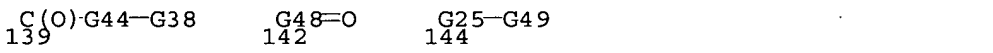
G37 = alkyl <containing 1-6 C> / F / Cl / Br / I / CN /
NO2 / CF3 / OCF3 / NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / 74 / 76 / 81 /
86 / OH / 94 / SH / 89 / 91 / 96 / 100 / 104 / 105 / 109 /
112 / 114 / 118 / 136 / 139 / carbocycle <containing 5-6 C,
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G47) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G47) / 142 / 144



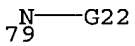




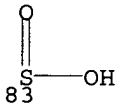




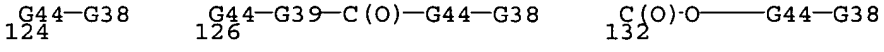
G38 = NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C>
G39 = NH / 79



G40 = H / alkyl <containing 1-6 C> / OH / alkoxy <containing 1-6 C>
G41 = 83 / alkylsulfonyl <containing 1-6 C>



G42 = (1-4) CH2
G43 = alkyl <containing 1-6 C> / 124 / 126 / 132



G44 = alkylene <containing 1-6 C>
G45 = cycloalkylene <containing 3-6 C>
G46 = OH / alkoxy <containing 1-6 C>
G47 = alkyl <containing 1-6 C> / F / Cl / Br / I / OH / CN / tetrazolyl / NH2 / CO2H / alkoxycarbonyl <containing 1-6 C>
G48 = carbocycle <containing 5-6 C,

5- to 6-membered monocyclic ring> (opt. substd.) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
5- to 6-membered monocyclic ring> (opt. substd.)
G49 = carbocycle <containing 5-6 C,
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G47) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G47) / 146

G48=O
146

G50 = CO2H / H / CO2Me / CN
Patent location: claim 1
Note: substitution is restricted
Note: additional interruptions in G14 and G32 also claimed
Note: and pharmaceutically acceptable salts and N-oxides
Stereochemistry: and isomers and racemic forms

L86 ANSWER 14 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:407108 MARPAT
TITLE: Process for synthesizing antifolates
INVENTOR(S): Xiao, Zejun; Kochat, Harry
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004092739	A1	20040513	US 2003-627485	20030725
WO 2004045500	A2	20040603	WO 2003-US33237	20031022
WO 2004045500	A3	20040826		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
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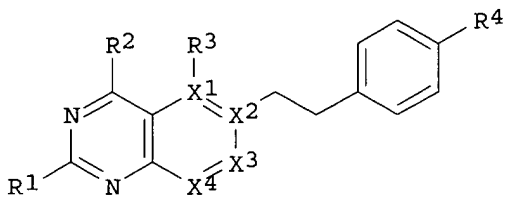
AU 2003287174	A1	20040615	AU 2003-287174	20031022

PRIORITY APPLN. INFO.:
US 2002-425826P 20021113
US 2003-627485 20030725
WO 2003-US33237 20031022

GI



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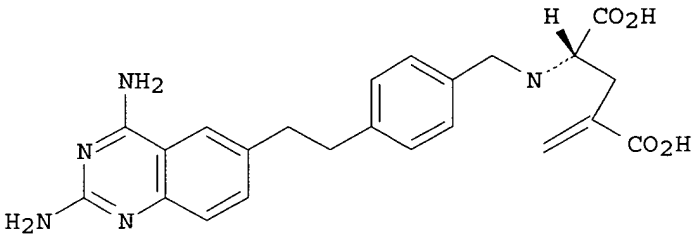
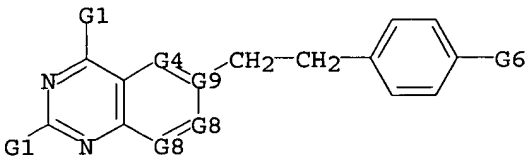


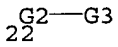
II

AB This invention relates to a process for synthesizing certain folic acid analogs [I; herein R1, R2 = amino or N-alkyl substituted amino, HO, alkoxy, keto, lower alkyl, or a nitrogen or oxygen protecting group; R3 = H, HO, alkoxy, CF3, alkoxy, halo, SH, or alkylthio; R4 = HO, alkoxy, CO-X; wherein X = HO, alkoxy, or an amino acid residue; X1-X4 = carbon or nitrogen], in particular γ-methylene glutamate 5,8,10-trideazaaminopterin (TRIDAM), (II) which are useful in treating cancer, inflammatory diseases, or autoimmune diseases, and are commonly referred to as antifolates (no data). The process employs improved steps for annulation, derivatization and addition reactions to produce the described antifolates from commonly available starting materials. Thus, a mixture of 2-amino-5-methylbenzonitrile and cyanoguanidine in 1 N aqueous HCl solution was heated at reflux for 1.5 h to give, after workup and treatment with aqueous ammonium hydroxide, 2,4-diamino-6-methylquinazoline which was amidated with benzoyl chloride in the presence of Et3N in 1,4-dioxane under heating at reflux for 1 h to give 2,4-dibenzamido-6-methylquinazoline (III). III was brominated by 1,3-dibromo-5,5-dimethylimidazolidine-2,4-dione in the presence of benzoyl peroxide in CCl4 under irradiation with a high intensity lamp (600 W, 120 V) for 1 h to give 2,4-dibenzamido-6-bromomethylquinazoline which was reacted with triphenylphosphine in THF under relaxing for 2 h and underwent Wittig reaction with Me 4-formylbenzoate in the presence of potassium tert-butoxide in THF at 25° for 24 h to give 2,4-Dibenzamido-6-[2-(p-methoxycarbonylphenyl)ethenyl]quinazoline (IV). IV was hydrogenated over 10% Pd-C in DMF at a hydrogen pressure of 20 psi for 20 h to give 2,4-Dibenzamido-6-[p-(methoxycarbonyl)phenethyl]quinazoline which was hydrolyzed in a mixture of 1 N aqueous KOH solution and MeCN under heating at reflux for 42 h and neutralized with AcOH to give 4-amino-4-deoxy-5,8,10-trideazapteroic acid (V). V was condensed with di-Et 4-methylene-L-glutamate hydrochloride in DMF at 25° for 30 min using 1-hydroxybenzotriazole and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride as condensing agents to give di-Et 4-methylene-N-[4-[2-(2,4-diaminoquinazolin-6-yl)ethyl]benzoyl]glutamate, i.e. TRIDAM di-Et ester, which was saponified in a mixture of 1 N aqueous NaOH solution and MeCN at 25° for 16 h and neutralized with AcOH to give TRIDAM II.

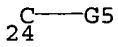
MSTR 1



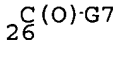
G1 = **NH2 (opt. substd.)** / **OH** / alkoxy / loweralkyl / R <"keto group"> / 22 / (Example: NHCOPh)



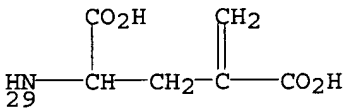
G2 = O / NH
G3 = R <"protecting group">
G4 = N / **24**

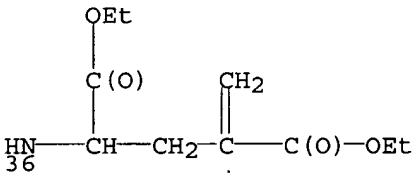


G5 = H / OH / alkoxy / CF3 / alkoxy / **halo** / SH / alkylthio
G6 = OH / alkoxy / 26 / (Example: OMe)



G7 = OH / alkoxy / R <"amino acid residue"> / (Examples: 29 / 36)





G8 = **CH** / **N**
G9 = **C** / 28

Patent location: claim 1

L86 ANSWER 15 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:350180 MARPAT
TITLE: Preparation of benzoxazinones and benzodioxanes as antibacterials.

INVENTOR(S): Surivet, Jean-Philippe; Zumbrunn, Cornelia; Hubschwerlen, Christian
PATENT ASSIGNEE(S): Morphochem A.-G. Aktiengesellschaft fuer Kombinatorische Chemie, Germany
SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10316081	A1	20041021	DE 2003-10316081	20030408
AU 2004228147	A1	20041021	AU 2004-228147	20040329
CA 2534891	AA	20041021	CA 2004-2534891	20040329
WO 2004089947	A2	20041021	WO 2004-EP3306	20040329
WO 2004089947	A3	20050106		

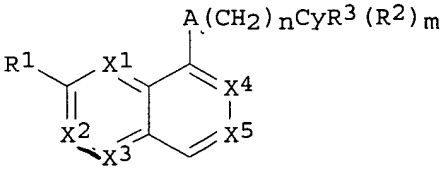
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1613624	A2	20060111	EP 2004-724014	20040329

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

PRIORITY APPLN. INFO.: DE 2003-10316081 20030408
WO 2004-EP3306 20040329

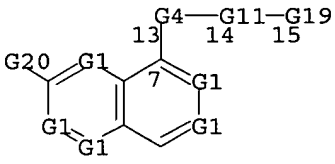
GI



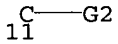
I

AB Title compds. (I; A = O, S, NH, alkylene, alkenylene, alkynylene, heteroalkylene; X1-X5 = N, CH, CR4; Cy = cycloalkylene, heterocycloalkylene, arylene, heteroarylene; R1 = H, halo, OH, amino, SH, alkyl, alkoxy, cycloalkyl, etc.; R2 = halo, OH, amino, NO2, SH, alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, etc.; R2R2 = atoms to form aryl, heteroaryl, cycloalkyl, heterocycloalkyl, etc. rings; R3 = alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, etc.; R4 = halo, OH, alkyl, alkenyl, alkynyl, heteroalkyl; m, n = 0-2), were prepared as antibacterials (no data). Thus, 4-(7-methoxynaphthalen-1-yloxymethyl)piperidine (preparation given), 6-(2-chloroacetyl)-4H-benzo[1,4]oxazin-3-one, and Et3N were heated 2 h at 50° in THF to give 52% coupling product, which was reduced with NaBH4 in EtOH to give 6-[1-hydroxy-2-[4-(7-methoxynaphthalen-1-ylooxymethyl)piperidin-1-yl]ethyl]-4H-benzo[1,4]dioxane.

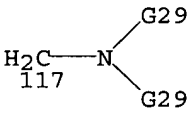
MSTR 1



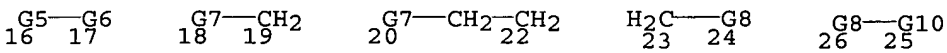
G1 = **N / 11**

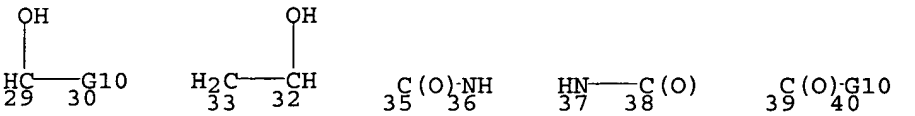


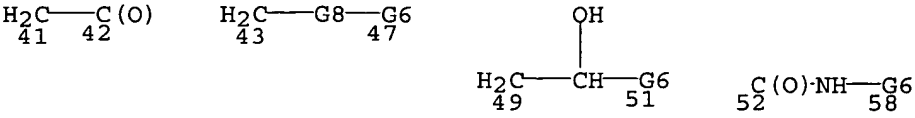
G2 = **F** / Cl / Br / I / H / **OH** /
carbon chain <containing 1-20 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by G3) /
R <"heteroalkyl group"> / (Specifically claimed: alkoxy <containing 1-4 C> (opt. substd. by 1 or more F) / 117)



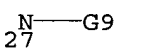
G3 = F / Cl / Br / I
G4 = O / S / NH / carbon chain <containing 1-20 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by G3) / R <"heteroalkylene group"> /
16-7 17-14 / 18-7 19-14 / 20-7 22-14 /
(Specifically claimed: G6 / 23-7 24-14 / 26-7 25-14 / CHOH / 29-7 30-14 / 33-7 32-14 / 35-7 36-14 /
37-7 38-14 / 39-7 40-14 / 41-7 42-14 / 43-7 47-14 /
49-7 51-14 / 52-7 58-14 / 54-7 59-14 / 56-7 60-14)



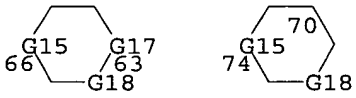




G5 = O / S / NH
G6 = (1-2) CH2
G7 = carbon chain <containing 1-20 C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by G3) / R <"heteroalkylene group">
G8 = O / S / 27



G9 = alkyl <containing 1-4 C>
G10 = (1-3) CH2
G11 = cycloalkylene <containing 3-14 C, non-aromatic>
(opt. substd. by (up to 2) G12) /
heterocycle <containing 3-14 atoms, zero or more O,
zero or more N, zero or more Si, zero or more Se,
zero or more S, zero or more P (no other heteroatoms),
non-aromatic> (opt. substd. by (up to 2) G12) /
arylene <containing 6-14 C> (opt. substd. by (up to 2) G12) /
heteroarylene <containing 5-14 atoms, zero or more O,
zero or more N, zero or more P,
zero or more S (no other heteroatoms)>
(opt. substd. by (up to 2) G12) /
(Specifically claimed: 66-13 63-15 / 74-13 70-15)



G12 = F / Cl / Br / I / OH / NH2 / NO2 / SH /
carbon chain <containing 1-20 C, 0 or more double bonds,
0 or more triple bonds> (opt. substd. by G3) /
R <"heteroalkyl group"> / aryl <containing 6-14 C>
(opt. substd. by G14) / heteroaryl <containing 5-14 atoms,
zero or more N, zero or more O, zero or more S,
zero or more P (no other heteroatoms)>
(opt. substd. by G14) / carbocycle <containing 3-14 C,
non-aromatic> (opt. substd. by G13) /
heterocycle <containing 3-14 atoms, zero or more O,
zero or more N, zero or more Si, zero or more Se,
zero or more P, zero or more S (no other heteroatoms),
non-aromatic> (opt. substd.)
G13 = R / carbon chain <containing 1-20 C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by G3) / R <"heteroalkyl residue">
G14 = R / carbon chain <containing 1-20 C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by G3) / carbocycle <containing 3-14 C,
non-aromatic> (opt. substd.)
G15 = N / 67

C—G16
67

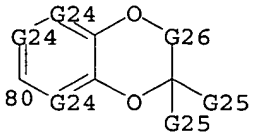
G16 = H / OH
G17 = N / CH
G18 = (0-1) CH2
G19 = carbon chain <containing 1-20 C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by G3) / R <"heteroalkyl group"> /
aryl <containing 6-14 C> (opt. substd. by G14) /
heteroaryl <containing 5-14 atoms, zero or more N,
zero or more O, zero or more S,
zero or more P (no other heteroatoms)>
(opt. substd. by G14) / carbocycle <containing 3-14 C,
non-aromatic> (opt. substd. by G13) /
heterocycle <containing 3-14 atoms, zero or more O,
zero or more N, zero or more Si, zero or more Se,
zero or more P, zero or more S (no other heteroatoms),
non-aromatic> (opt. substd.) / (Specifically claimed: 78)

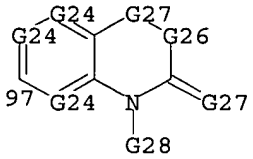
G22—G23
78

G20 = H / F / Cl / Br / I / OH / **NH2** / SH /
alkyl <containing 1-20 C> (opt. substd.) /
R <"heteroalkyl group"> / 76 / carbocycle <containing 3-14
C, non-aromatic> (opt. substd. by G13) /
heterocycle <containing 3-14 atoms, zero or more O,
zero or more N, zero or more Si, zero or more Se,
zero or more P, zero or more S (no other heteroatoms),
non-aromatic> (opt. substd.) / (Specifically claimed: OMe)

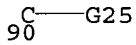
O—G21
76

G21 = alkyl <containing 1-20 C> (opt. substd. by G3) /
R <"heteroalkyl group"> / carbocycle <containing 3-14 C,
non-aromatic> (opt. substd. by G13) /
heterocycle <containing 3-14 atoms, zero or more O,
zero or more N, zero or more Si, zero or more Se,
zero or more P, zero or more S (no other heteroatoms),
non-aromatic> (opt. substd.)
G22 = carbon chain <containing 1-20 C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by G3) / R <"heteroalkylene group">
G23 = aryl <containing 6-14 C> (opt. substd. by G14) /
heteroaryl <containing 5-14 atoms, zero or more N,
zero or more O, zero or more S,
zero or more P (no other heteroatoms)>
(opt. substd. by G14) / carbocycle <containing 3-14 C,
non-aromatic> (opt. substd. by G13) /
heterocycle <containing 3-14 atoms, zero or more N,
zero or more O, zero or more S, zero or more P,
zero or more Si, zero or more Se (no other heteroatoms),
non-aromatic> (opt. substd.) / 80 / 97

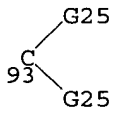




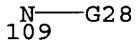
G24 = N / 90



G25 = H / F / Cl / Br / I / OH /
carbon chain <containing 1-20 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by G3) /
R <"heteroalkyl group">
G26 = (0-2) 93



G27 = O / S / 109



G28 = H / carbon chain <containing 1-20 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by G3) / R <"heteroalkyl residue">
G29 = alkyl <containing 1-5 C>
Patent location: claim 1

L86 ANSWER 16 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 139:164803 MARPAT
TITLE: Preparation of condensed heterocyclic compounds as PARP inhibitors
INVENTOR(S): Ishida, Junya; Hattori, Kouji; Kido, Yoshiyuki; Yamamoto, Hirofumi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063874	A1	20030807	WO 2003-JP708	20030127

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,

G11 = **27** / **(1-3) N**

C——G12
27

G12 = H / R / (Specifically claimed: alkoxy <containing 1-4 C> / **F** / Cl / Br / I / NH2 / alkylamino <containing 1-4 C> / dialkylamino <each alkyl containing 1-4 C> / NHNH2 / alkyl <containing 1-4 C> / OH)
G13 = 38 / (up to 1) N

C——G12
38

G14 = NH / O / S
G15 = 58 / (up to 1) N

C——G12
58

G16 = 60 / (up to 1) N

C——G12
60

G17 = (1-2) CH2
G18 = N / CH
G19 = O / S / NH / 149

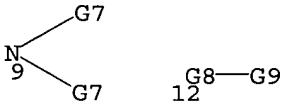
N——G2
149

G20 = H / alkyl <containing 1-4 C> / **NH2** / alkylamino <containing 1-4 C> / dialkylamino <each alkyl containing 1-4 C>
Derivative: or pharmaceutical salts or hydrates
Patent location: claim 1
Note: substitution is restricted; additional ring formation is allowed; also incorporates claim 75
Stereochemistry: and stereoisomers

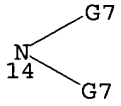
L86 ANSWER 26 OF 26 BEILSTEIN COPYRIGHT 2006 BEILSTEIN MDL on STN

Beilstein Records (BRN): 573824
Chemical Name (CN): 3-azido-2-methyl-5-phenyl-2H-pyrimido<4,5-c>quinolin-1-one
Autonom Name (AUN): 3-azido-2-methyl-5-phenyl-2H-pyrimido<4,5-c>quinolin-1-one
Molec. Formula (MF): C18 H12 N6 O

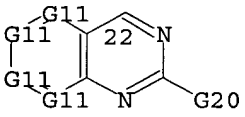
alkoxycarbonyl <containing 1-4 C> /
cycloalkyloxycarbonyl <containing 3-8 C> /
alkenyl <containing 2-4 C> / cycloalkenyl <containing 4-8 C>
/ alkynyl <containing 2-4 C>

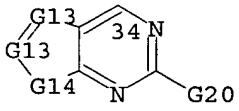


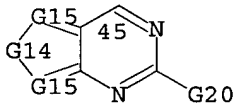
G7 = cycloalkyl <containing 3-8 C>
G8 = SO2 / C(O)
G9 = NH2 / alkylamino <containing 1-4 C> /
dialkylamino <each alkyl containing 1-4 C> /
cycloalkylamino <containing 3-8 C> / 14

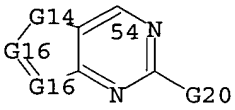


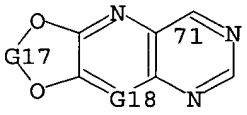
G10 = **22** / 34 / 45 / 54 / (Specifically claimed: 71 / 80 /
94 / 114 / 123 / 138)

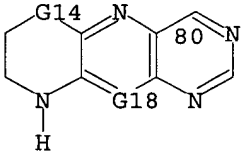


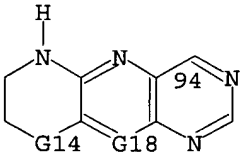


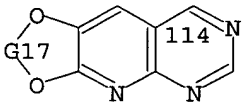


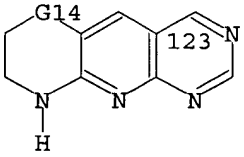


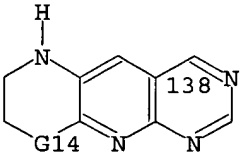












(dimethylamino)pyrido[3,4-d]pyrimidine, which demonstrated a IC50 of 6 pM for inhibition of tyrosine kinase at an epidermal growth factor receptor.

MSTR 1

```
G10—G1—G5
1     3
```

G1 = **O** / S / NH / 5 / 148-1 4-3

```
 G19—G3    N——G2
148  4    5
```

G2 = alkyl <containing 1-4 C> / OH / NH2 /
alkoxy <containing 1-4 C> / alkylamino <containing 1-4 C>
G3 = (1-2) 7

```
HC——G4
7
```

G4 = H / alkyl <containing 1-4 C>
G5 = Ph (opt. substd. by (1-3) G6) / thienyl / furyl /
pyrrolyl / pyridyl / pyrimidinyl / imidazolyl / pyrazinyl /
oxazolyl / thiazolyl / naphthyl / benzothienyl /
benzofuranyl / indolyl / quinolinyl / isoquinolinyl /
quinazolinyl / carbocycle <containing 10 C, aromatic,
bonds all normalized, bicyclic, (2) 6-membered rings>
(opt. substd. by (1-3) G6) / heterocycle <containing 1-2
heteroatoms, zero or more N, up to 1 O,
up to 1 S (no other heteroatoms), aromatic, 2 double bonds,
5-membered monocyclic ring> (opt. substd. by (1-3) G6) /
heterocycle <containing 1-2 heteroatoms,
1-2 N (no other heteroatoms), aromatic,
bonds all normalized, mono- or bicyclic,
(1-2) 6-membered rings only> (opt. substd. by (1-3) G6) /
heterocycle <containing 1 heteroatom, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
aromatic, 6 normalized bonds, 1 double bond, bicyclic,
(1) 5-membered ring, (1) 6-membered ring>
(opt. substd. by (1-3) G6)
G6 = alkyl <containing 1-4 C> /
cycloalkyl <containing 3-8 C> / alkoxy <containing 1-4 C> /
cycloalkyloxy <containing 3-8 C> / NO2 / F / Cl / Br / I /
perfluoroalkyl <containing 1-4 C> / OH /
alkylcarbonyloxy <containing 1-4 C> /
cycloalkylcarbonyloxy <containing 3-8 C> / NH2 /
alkylamino <containing 1-4 C> /
dialkylamino <each alkyl containing 1-4 C> /
cycloalkylamino <containing 3-8 C> / 9 / CH2OH /
alkylcarbonyl <containing 1-4 C> /
cycloalkylcarbonyl <containing 3-8 C> / CN /
alkylthio <containing 1-4 C> / alkylsulfinyl <containing 1-4
C> / alkylsulfonyl <containing 1-4 C> /
cycloalkylthio <containing 3-8 C> /
cycloalkylsulfinyl <containing 3-8 C> /
cycloalkylsulfonyl <containing 3-8 C> / 12 / SH / CO2H /

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9519774	A1	19950727	WO 1995-US941	19950123
W: AM, AU, BG, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SI, SK, TJ, UA, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5654307	A	19970805	US 1994-358351	19941223
ZA 9500440	A	19951010	ZA 1995-440	19950119
AU 9517314	A1	19950808	AU 1995-17314	19950123
AU 686334	B2	19980205		
EP 742717	A1	19961120	EP 1995-909316	19950123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09508127	T2	19970819	JP 1995-519732	19950123
PL 179132	B1	20000731	PL 1995-315633	19950123
MD 1632	F2	20010331	MD 1996-217	19950123
RU 2174980	C2	20011020	RU 1996-116985	19950123
RO 117257	B1	20011228	RO 1996-1517	19950123
NZ 281011	A	20020201	NZ 1995-281011	19950123
BG 63245	B1	20010731	BG 1996-100614	19960520
FI 9602856	A	19960925	FI 1996-2856	19960715
FI 114213	B1	20040915		
NO 9603094	A	19960724	NO 1996-3094	19960724
NO 309892	B1	20010417		
FI 2004000648	A	20040507	FI 2004-648	20040507
FI 2004000649	A	20040507	FI 2004-649	20040507
PRIORITY APPLN. INFO.:			US 1994-186735	19940125
			US 1994-186745	19940125
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			WO 1995-US941	19950123

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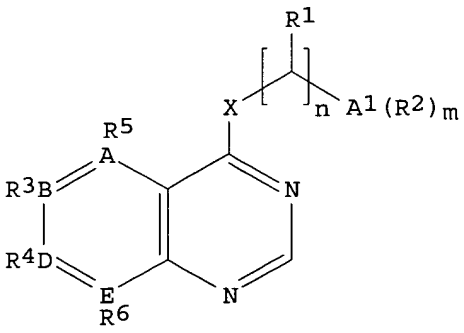
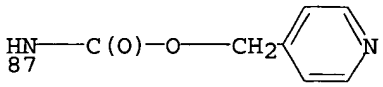
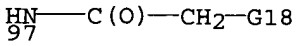
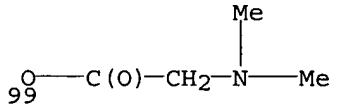


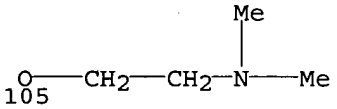
I

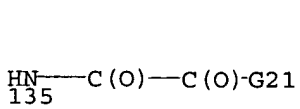
AB The title compds. [I; A-E = nitrogen with the remaining atom(s) carbon, or any two contiguous positions in A-E taken together can be a single heteroatom N, O or S, in which case one of the two remaining atoms must be carbon, and the other can be either carbon or nitrogen, etc.; A1 = divalent Ph, thienyl, furanyl pyrimidinyl, heterocyclyl, etc.; R1 = H, lower alkyl; R2 = lower alkyl, cycloalkyl, alkoxy, cycloalkoxy, NO2, halogen, etc.; R3-R6 = H, alkyl, alkoxy, HO, acyloxy, (un)substituted NH2, etc.; X = O, S, (un)substituted NH; m = 0-3; n = 0-2], useful for inhibiting tyrosine kinases of the epidermal growth factor receptor family, are prepared Thus, 4-(3-bromoanilino)-6-fluoropyrido[3,4-d]pyrimidine was reacted with Me2NH, producing 4-(3-bromoanilino)-6-



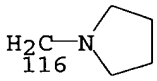


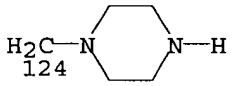


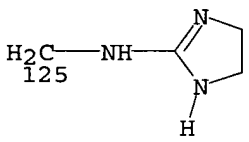


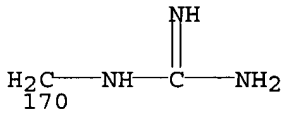


G18 = morpholino / NMe2 / piperazino / pyrrolidino
G20 = Cl / F / Br / Me / Et / Pr-i / OMe / OH / NH2 / CF3 / OCF3 / SMe / OMe / CO2H / CO2Me / CH2NH2 / NMe2 / 116 / CH2OH / (Specifically claimed: 124 / NHC(NH)NH2 / 170 / 125)

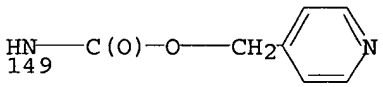


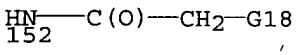


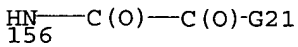


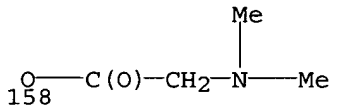


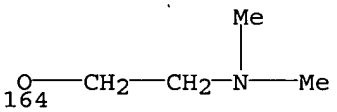
G21 = morpholino / piperazino / pyrrolidino
G22 = H / Cl / F / Br / Me / OMe / OH / CF3 / OCF3 / OPr-n / NH2 / NMe2 / NHSO2Ph / 149 / 152 / 156 / 158 / 164





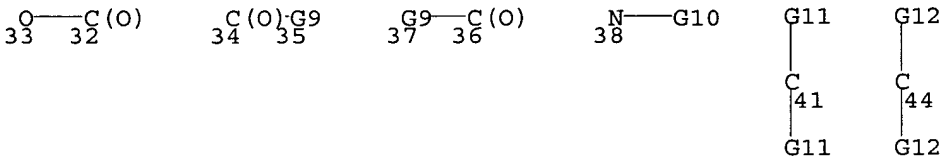




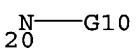


Derivative: or pharmaceutically acceptable salts
Patent location: claim 1
Note: additional ring formation also claimed

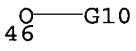
L86 ANSWER 25 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 124:8839 MARPAT
TITLE: Preparation of bicyclic pyrimidines capable of inhibiting tyrosine kinases of the epidermal growth factor receptor family
INVENTOR(S): Bridges, Alexander James; Denny, William Alexander; Fry, David; Kraker, Alan; Meyer, Robert; Rewcastle, Gordon William; Thompson, Andrew Mark
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: PCT Int. Appl., 218 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4



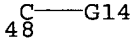
G9 = **NH** / 20



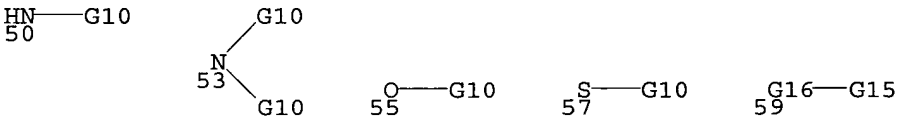
G10 = alkyl <containing 1-3 C> (opt. substd.) /
alkenyl <containing 2-3 C> (opt. substd.)
G11 = H / alkyl <containing 1-3 C> (opt. substd.) /
alkenyl <containing 2-3 C> (opt. substd.)
G12 = OH / 46

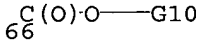


G13 = **N** / **48**

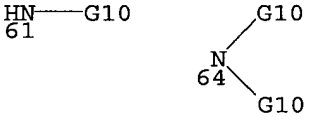


G14 = H / alkyl <containing 1-3 C> (opt. substd.) /
alkenyl <containing 2-3 C> (opt. substd.) / NH2 / 50 / 53 /
OH / 55 / SH / 57 / 59 / CO2H / 66 /
(Specifically claimed: Me)

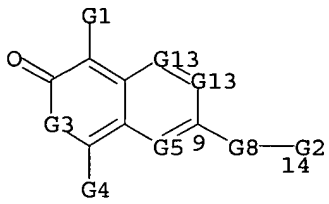




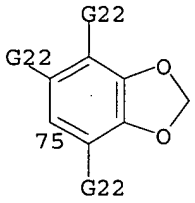
G15 = NH2 / 61 / 64



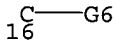
G16 = C(O) / SO2
G17 = Cl / F / Br / Me / OMe / OH / CF3 / OCF3 / OPr-n /
NH2 / NMe2 / NHSO2Ph / 87 / 97 / 135 / 99 / 105



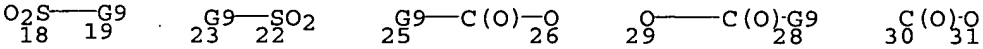
G1 = Ph (opt. substd.) / heterocycle <containing 5-6 atoms, aromatic, 5- to 6-membered monocyclic ring> (opt. substd.) / aryl <containing 8-10 C, bicyclic> (opt. substd.) / heterocycle <containing 8-10 atoms, aromatic, bicyclic> (opt. substd.) / (Specifically claimed: Ph (opt. substd. by (1-3) G17) / pyridyl (opt. substd. by (1-3) G17) / 75)



G2 = Ph (opt. substd.) / heterocycle <containing 5-6 atoms, aromatic, 5- to 6-membered monocyclic ring> (opt. substd.) / aryl <containing 8-10 C, bicyclic> (opt. substd.) / heterocycle <containing 8-10 atoms, aromatic, bicyclic> (opt. substd.) / (Specifically claimed: Ph (opt. substd. by (1-3) G20) / pyridyl (opt. substd. by (1-3) G20))
G3 = O / **NH (opt. substd.)**
G4 = H / alkyl <containing 1-3 C> / OH / **alkoxy <containing 1-3 C>**
G5 = **N** / 16



G6 = H / alkyl <containing 1-3 C> / alkenyl <containing 2-3 C> / alkynyl <containing 2-3 C> / Ph (opt. substd. by (1-3) G7)
G7 = halo / OMe / CN / NO2 / NH2 / OH / Me / Et
G8 = S / O / SO2 / S(O) / **18-9 19-14** / 23-9 22-14 / 25-9 26-14 / 29-9 28-14 / C(O) / 30-9 31-14 / 33-9 32-14 / 34-9 35-14 / 37-9 36-14 / NH / 38 / 41 / 44



TITLE: Heterocyclic compound inhibitors of p38 kinase, pharmaceutical compositions, and therapeutic use
INVENTOR(S): Salituro, Francesco; Bemis, Guy; Cochran, John
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964400	A1	19991216	WO 1999-US12951	19990611
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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AU 9944297	A1	19991230	AU 1999-44297	19990611
EP 1086085	A1	20010328	EP 1999-927377	19990611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1277740	A1	20030122	EP 2002-22891	19990611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 2001025044	A1	20010927	US 2000-734069	20001211
US 6528508	B2	20030304		
US 2003149037	A1	20030807	US 2002-327020	20021220
US 6800626	B2	20041005		
US 2005049251	A1	20050303	US 2004-951409	20040927
PRIORITY APPLN. INFO.:			US 1998-89147P	19980612
			EP 1999-927377	19990611
			WO 1999-US12951	19990611
			US 2000-734069	20001211
			US 2002-327020	20021220

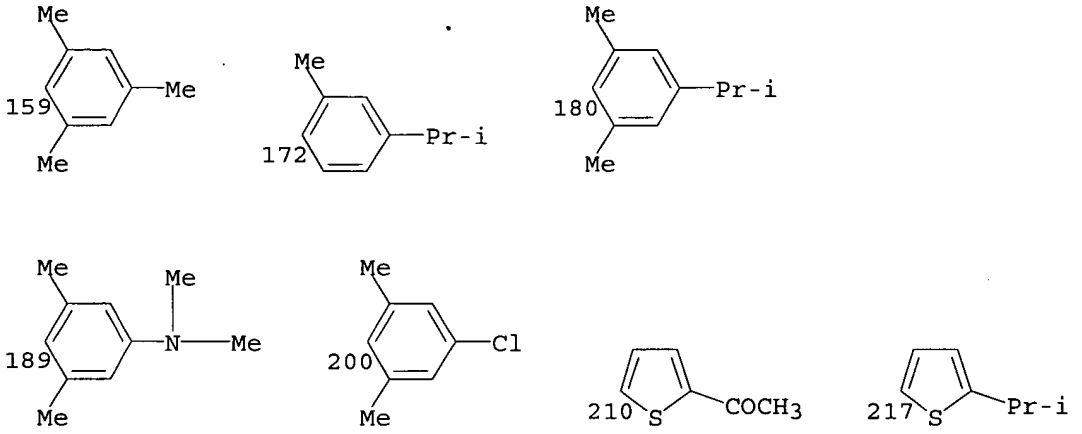
AB The invention relates to heterocyclic compound inhibitors of p38, a mammalian protein kinase involved cell proliferation, cell death and response to extracellular stimuli. The invention also relates to methods for producing these inhibitors. The invention also provides pharmaceutical compns. comprising the inhibitors of the invention and methods of utilizing those compns. in the treatment and prevention of various disorders.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

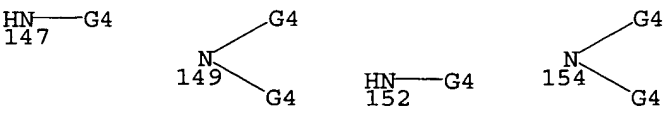
MSTR 1A

G15 = 88 / 89

G16 = heteroaryl (opt. substd. by (1-3) G17) /
aryl (opt. substd. by (1-3) G17) /
(Specifically claimed: 159) / (Examples: Ph / naphthyl /
pyridyl / thienyl / furyl / pyrimidinyl / pyrazinyl / 172 /
180 / 189 / 200 / 210 / 217 / 222 / 231)

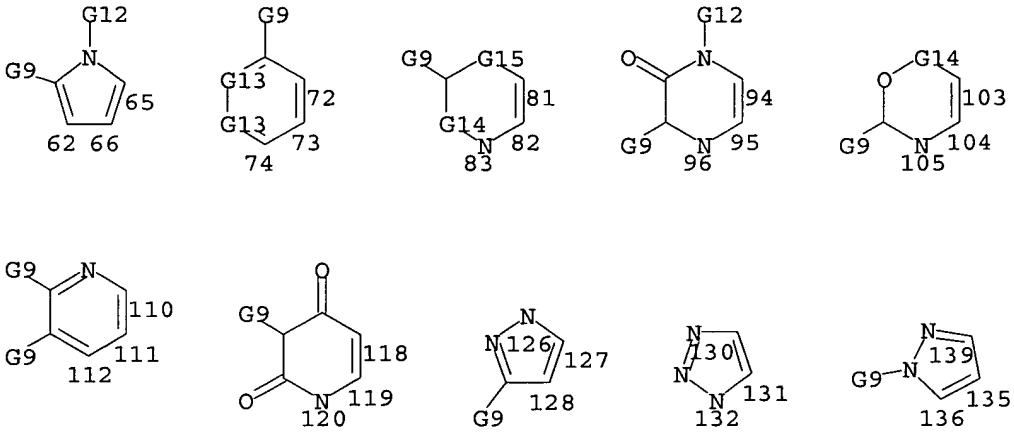


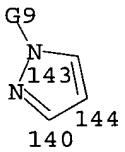
G17 = F / Cl / Br / alkyl <containing 1-5 C>
(opt. substd. by OH) / alkoxy <containing 1-4 C> /
alkyl <containing 1-5 C> (substd. by (1-3) G10) / OH / SH /
alkylthio <containing 1-4 C> / alkylcarbonyl <containing 1-4
C> / NH2 / 147 / 149 / alkyl <containing 1-4 C>
(substd. by alkoxy <containing 1-4 C>) /
alkyl <containing 1-4 C> (substd. by NH2) /
alkyl <containing 1-5 C> (substd. by 152) /
alkyl <containing 1-5 C> (substd. by 154) / NO2



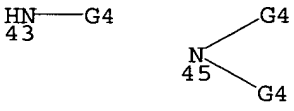
Patent location: claim 1

L86 ANSWER 24 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 132:30857 MARPAT

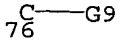




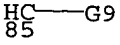
G9 = H / **F** / Cl / Br / alkyl <containing 1-5 C> (opt. substd. by OH) / cycloalkyl <containing 3-8 C> / alkoxy <containing 1-4 C> / alkylcarbonyl <containing 1-4 C> / aryl (opt. substd.) / heteroaryl / alkylthio <containing 1-4 C> / alkyl <containing 1-5 C> (substd. by (1-3) G10) / alkyl <containing 1-4 C> (substd. by alkoxy <containing 1-4 C>) / alkyl <containing 1-5 C> (substd. by 43) / alkyl <containing 1-5 C> (substd. by 45) / NO2 / (Specifically claimed: Me)

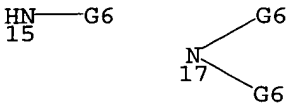


G10 = F / Cl / Br
G11 = CH=CHCH=CH / CH2CH2CH2CH2
G12 = H / alkyl <containing 1-10 C> / alkyl <containing 1-4 C> (substd. by cycloalkyl <containing 3-8 C>) / cycloalkyl <containing 3-8 C>
G13 = **76** / **N**

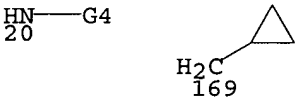


G14 = C(O) / 85

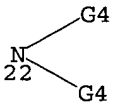




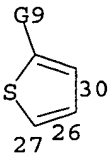
G6 = alkyl <containing 1-10 C> /
alkyl <containing 1-4 C> (substd. by cycloalkyl <containing 3-8 C>) / cycloalkyl <containing 3-8 C> /
aryl (opt. substd.) / heteroaryl /
alkyl <containing 1-5 C> (substd. by OH) /
alkyl <containing 1-5 C> (substd. by 1 or more aryl (opt. substd.)) / alkyl <containing 1-5 C>
(substd. by heteroaryl) / alkylcarbonyl <containing 1-4 C> /
alkyl <containing 1-4 C> (substd. by alkoxy <containing 1-4 C>) / alkyl <containing 1-4 C> (substd. by alkylthio <containing 1-4 C>) / alkyl <containing 1-4 C>
(substd. by NH2) / alkyl <containing 1-5 C> (substd. by 20) /
alkyl <containing 1-5 C> (substd. by G7) /
alkyl <containing 1-3 C> (substd. by CO2H) /
alkyl <containing 1-3 C> (substd. by alkoxycarbonyl <containing 1-3 C>) / (Specifically claimed: Et / Bu-n / Pr-n / 169)

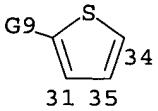


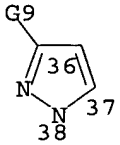
G7 = 22 / heterocycle <containing 1 heteroatom, 1 N, attached through 1 N, 4- to 6-membered monocyclic ring>

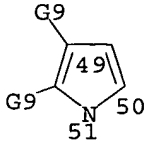


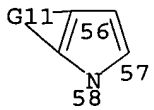
G8 = 30-4 26-2 27-25 / 34-4 35-2 31-25 /
36-4 37-2 38-25 / 49-4 50-2 51-25 / 56-4 57-2 58-25 /
65-4 66-2 62-25 / **72-4 73-2 74-25** / 81-4 82-2 83-25 /
94-4 95-2 96-25 / 103-4 104-2 105-25 /
110-4 111-2 112-25 / 118-4 119-2 120-25 /
126-4 127-2 128-25 / 130-4 131-2 132-25 /
139-4 135-2 136-25 / 143-4 144-2 140-25









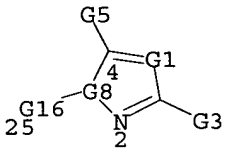


PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000038350	A2	20000208	JP 1999-136173	19990517
PRIORITY APPLN. INFO.:			JP 1998-135673	19980518

AB Pyrimidine derivs. (Markush's structures given), including 4-(N-butyl-N-ethylamino)-2,5-di-methyl-7-(2,4,6-trimethylphenyl)-thieno[3,4-d]pyrimidine, and their pharmaceutically acceptable salts and hydrates are claimed as antidiabetics by acting as CRF antagonists. The hypoglycemic, insulin secretion-promoting, and insulin-enhancing effects were tested, and a formulation example of tablets was given.

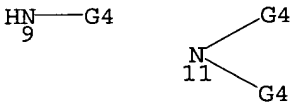
MSTR 1



G1 = **N** / 6

G2 = H / alkyl <containing 1-5 C> / F / Cl / Br / CN / OH / alkoxy <containing 1-4 C>

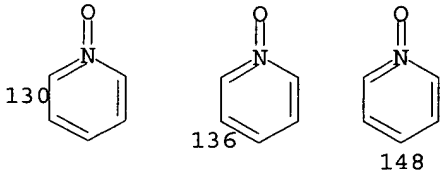
G3 = H / alkyl <containing 1-5 C> (opt. substd. by OH) / alkyl <containing 1-4 C> (substd. by cycloalkyl <containing 3-8 C>) / cycloalkyl <containing 3-8 C> / alkoxy <containing 1-4 C> / **NH2** / 9 / 11 / alkyl <containing 1-5 C> (substd. by (1-3) G10) / alkyl <containing 1-5 C> (substd. by 1 or more aryl (opt. substd.)) / alkyl <containing 1-4 C> (substd. by alkoxy <containing 1-4 C>) / OH / aryl (opt. substd.) / heteroaryl / F / Cl / Br / SH / alkylthio <containing 1-4 C> / (Specifically claimed: Me)



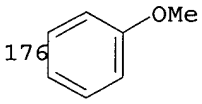
G4 = alkyl <containing 1-5 C> / cycloalkyl <containing 3-8 C>

G5 = NH2 / 15 / 17 / heterocycle <containing 1 or more heteroatoms, 1 or more N, attached through 1 or more N> / **alkoxy <containing 1-10 C>** / alkoxy <containing 1-4 C> (substd. by cycloalkyl <containing 3-8 C>) / cycloalkyloxy <containing 3-8 C>

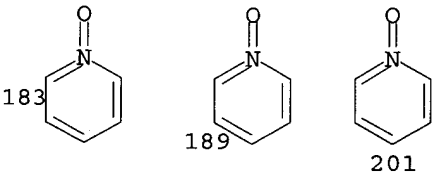
G23—G10
127



G18 = alkylene <containing 1 or more C> (opt. substd.)
G19 = O / NH
G20 = 2-pyridyl / Ph / 176



G21 = Ph (opt. substd.) / naphthyl / biphenylyl / 183 / 189 / 201 / carbocycle <containing 5-10 C, mono- or bicyclic> (opt. substd. by 1 or more G12) / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, zero or more O, zero or more S, zero or more N (no other heteroatoms), 1 or more C, mono- or bicyclic> / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, 1-4 N (no other heteroatoms), 1 or more C, mono- or bicyclic> (substd. by 1 or more G12) / alkyl <containing 1 or more C> (opt. substd.) / CF3 / cycloalkyl <containing 3-7 C> (opt. substd. by aryl <containing 6-14 C>) / cycloalkyl <containing 7-16 C, 2-3 rings>

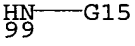


G22 = R / F
G23 = R <"linking group"> / alkylene <containing 1 or more C> (opt. substd.)
Patent location: claim 1
Note: or pharmaceutically acceptable salts
Note: substitution is restricted

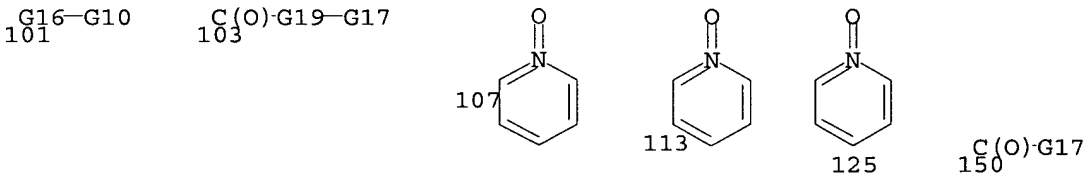
L86 ANSWER 23 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 132:146643 MARPAT
TITLE: Pyrimidine CRF antagonists as antidiabetics
INVENTOR(S): Seio, Yasushi; Tanaka, Hiroshi; Goto, Shinji; Amano, Yusaku
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

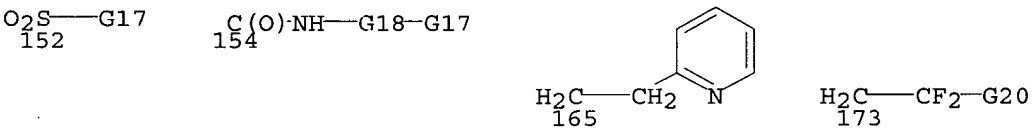
zero or more N (no other heteroatoms)>

G14 = NH2 / 99



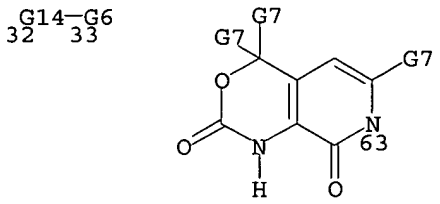
G15 = Ph (opt. substd. by 1 or more G11) / naphthyl / biphenylyl / 107 / 113 / 125 / carbocycle <containing 5-10 C, mono- or bicyclic> (opt. substd. by 1 or more G12) / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, zero or more O, zero or more S, zero or more N (no other heteroatoms), 1 or more C, mono- or bicyclic> / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, 1-4 N (no other heteroatoms), 1 or more C, mono- or bicyclic> (substd. by 1 or more G12) / alkyl <containing 1-7 C> (opt. substd. by 1 or more G13) / CF3 / cycloalkyl <containing 3-7 C> (opt. substd. by aryl <containing 6-14 C>) / cycloalkyl <containing 7-16 C, 2-3 rings> / 101 / 103 / 150 / 152 / 154 / (Specifically claimed: 165 / 173 / CH2CH2Ph)



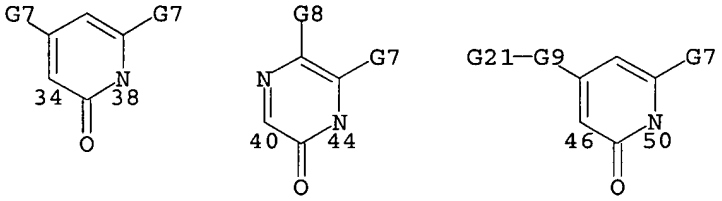


G16 = R <"linking group"> / alkylene <containing 1 or more C> (opt. substd. by 1 or more G22)

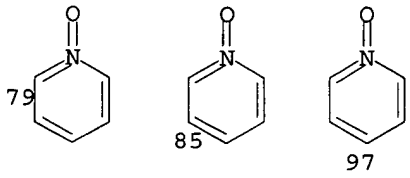
G17 = Ph (opt. substd.) / naphthyl / biphenylyl / 130 / 136 / 148 / carbocycle <containing 5-10 C, mono- or bicyclic> (opt. substd. by 1 or more G12) / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, zero or more O, zero or more S, zero or more N (no other heteroatoms), 1 or more C, mono- or bicyclic> / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, 1-4 N (no other heteroatoms), 1 or more C, mono- or bicyclic> (substd. by 1 or more G12) / alkyl <containing 1 or more C> (opt. substd.) / CF3 / cycloalkyl <containing 3-7 C> (opt. substd. by aryl <containing 6-14 C>) / cycloalkyl <containing 7-16 C, 2-3 rings> / 127



G6 = 34-32 38-2 / 40-32 44-2 / 46-32 50-2



G7 = H / F / Cl / Br / I / alkyl <containing 1-4 C> / cycloalkyl <containing 3-7 C> / CF3 / (Specifically claimed: Me / Pr-i / Et)
G8 = H / F / Cl / Br / I
G9 = CH2 / S / SO2
G10 = Ph (opt. substd. by 1 or more G11) / naphthyl / biphenylyl / 79 / 85 / 97 / carbocycle <containing 5-10 C, mono- or bicyclic> (opt. substd. by 1 or more G12) / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, zero or more O, zero or more S, zero or more N (no other heteroatoms), 1 or more C, mono- or bicyclic> / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, 1-4 N (no other heteroatoms), 1 or more C, mono- or bicyclic> (substd. by 1 or more G12) / alkyl <containing 1-7 C> (opt. substd. by 1 or more G13) / CF3 / cycloalkyl <containing 3-7 C> (opt. substd. by aryl <containing 6-14 C>) / cycloalkyl <containing 7-16 C, 2-3 rings>



G11 = alkyl <containing 1-4 C> / alkoxy <containing 1-4 C> / F / Cl / Br / I / OH / CO2H / CONH2 / CH2OH / alkoxycarbonyl <containing 1-4 C> / SO2NH2
G12 = F / Cl / Br / I / OH
G13 = OH / CO2H / NH2 / aryl <containing 6-14 C> / cycloalkyl <containing 3-7 C> / CF3 / NMe2 / alkyl <containing 1-3 C> (substd. by 1 or more aryl <containing 6-14 C>) / heteroaryl <containing 5-10 atoms, zero or more O, zero or more S, zero or more N (no other heteroatoms)> / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, zero or more O, zero or more S,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2403558	AA	20010927	CA 2001-2403558	20010319
EP 1267876	A1	20030102	EP 2001-918822	20010319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003527426	T2	20030916	JP 2001-568427	20010319
US 2002006923	A1	20020117	US 2001-815404	20010322
US 6534510	B2	20030318		
PRIORITY APPLN. INFO.:			US 2000-191559P	20000323
			WO 2001-US8733	20010319

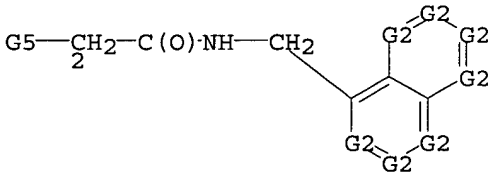
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

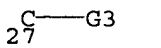
AB Heterocyclic compds. I (T = N or CY1, NH or CY1Y2 and N = 0, 1, 2 and Y1 and Y2 are independently H, C1-4 alkyl, halogen, NH2, OH; A = a-d; W = H, R1, R1OCO, R1CO, R1SO2, R1(CH2)nNHCO, (R1)2CH(CH2)nNHCO where n = 0-4 and R1 = (non)heterocyclic; R4 = Ph (un)substituted with one or more C1-4 alkyl(alkoxy), halogen, OH, CO2H, CONH2, CH2OH, naphthyl, biphenyl, pyridine N-oxide, (un)saturated (non)heterobicyclic ring, C1-7 alkyl (un)substituted with OH, CO2H, NH2, CF3, NMe2, etc.; R3, R5, and R6 = independently H, halogen, C1-4 alkyl, C3-7 cycloalkyl, CF3; X = H, halogen; Z = CH2, S, SO2) were prepared as thrombin inhibitors (no data). Thus II was prepared from 8-aminomethyl-1,2,3,4-tetrahydronaphthyridine and III in DMF, HOAt and EDC. Oral dosages of the thrombin inhibitors will range between 0.01 mg/kg of body weight per day to about 30 mg/kg/day.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1A



G2 = **N / 27**



G3 = H / alkyl <containing 1-4 C> / **F** / Cl / Br / I / **NH2 / OH**
G5 = 33 / 63

G16 = **19** / N

C——G4
19

G17 = S / S(O) / SO2
G18 = NH2 / 36 / heterocycle <containing 1 or more N, zero or more O, zero or more S (no other heteroatoms), attached through 1 N, mono- or polycyclic>

G9——G8
36

G19 = OH / 40 / NH2 / 42 / heterocycle <containing 1 or more N, zero or more O, zero or more S (no other heteroatoms), attached through 1 N, mono- or polycyclic>

O——G7 G9——G8
40 42

G20 = OH / 46

O——G7
46

G21 = O / S / S(O) / SO2
G22 = SO2 / C(O)
Patent location: claim 1
Note: and tautomers, and pharmaceutically acceptable salts, prodrugs and solvates
Note: additional ring formation also claimed
Note: addtional oxo formation also claimed
Stereochemistry: and isomers, enantiomers, diastereomers

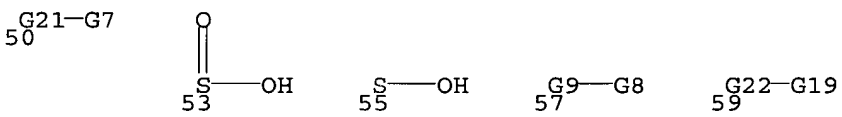
L86 ANSWER 22 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 135:272974 MARPAT
TITLE: Preparation of heterocyclic compounds as thrombin inhibitors
INVENTOR(S): Barrow, James C.; Dorsey, Bruce D.; Selnick, Harold G.; Ngo, Phung L.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070229	A1	20010927	WO 2001-US8733	20010319

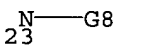
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

G3 = H / OH / halo / CN / 44 / NH2 / 48 /
heterocycle <containing 1 or more N, zero or more O, zero or more S (no other heteroatoms), attached through 1 N, mono- or polycyclic> / alkyl <containing 1-12 C> (opt. substd.) / alkenyl <containing 2-12 C> (opt. substd.) / alkynyl <containing 2-12 C> (opt. substd.) / carbocycle <containing 3 or more C, 0 or more double bonds, mono- or polycyclic> (opt. substd.) / heterocycle <containing 3 or more atoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or polycyclic>

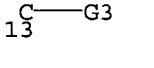
G4 = H / **halo** / NO2 / CN / 50 / OH / SH / 53 / 55 / NH2 / 57 / heterocycle <containing 1 or more N, zero or more O, zero or more S (no other heteroatoms), attached through 1 N, mono- or polycyclic> / 59 / alkylcarbonyl <containing 1-12 C> (opt. substd.) / carbon chain <containing 1-12 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)



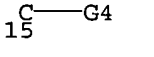
G7 = R
G8 = R
G9 = NH / 23



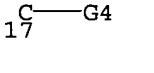
G10 = R
G11 = **C(O)** / S(O) / SO2
G12 = 13 / **N**

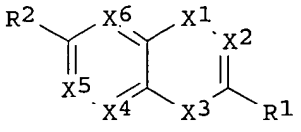


G13 = **NH** / O / S
G14 = **15** / N



G15 = 17 / **N**





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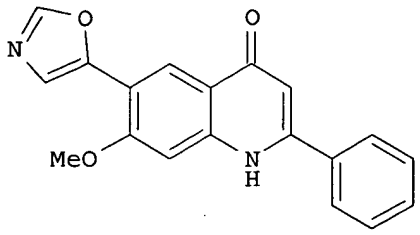
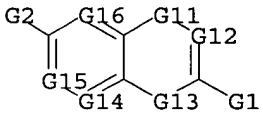


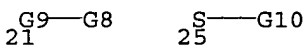
II

AB Title compds. I [wherein X1 = CO, SO, or SO2; X2 = CR3 or N; X3 = NH, O, or S; X4 = CR4 or N; X5 = CR5 or N; X6 = CR6 or N] were prepared were prepared as inosine monophosphate dehydrogenase (IMPDH) enzyme inhibitors. For example, acetalization of 4-nitro-2-methoxytoluene with AcOH (51%), reduction to the aldehyde (91%), and cycloaddn. with (p-tolylsulfonyl)methyl isocyanate gave 5-(4-nitro-2-methoxyphenyl)oxazole (84%), which was reduced to the amine (95%). Alkylation with Et benzoylacetate and cyclization afforded the 6-(5-oxazolyl)-4(1H)-quinolinone II. Thus, I are useful as therapeutic agents for IMPDH-associated disorders, such as allograft rejection (no data).

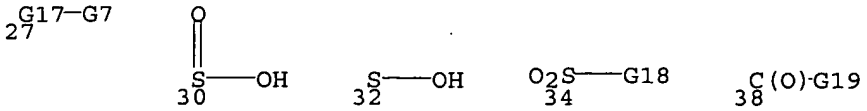
MSTR 1



G1 = alkyl <containing 1-12 C> (opt. substd.) / alkenyl <containing 2-12 C> (opt. substd.) / alkynyl <containing 2-12 C> (opt. substd.) / **NH2** / 21 / heterocycle <containing 1 or more N, zero or more O, zero or more S (no other heteroatoms), attached through 1 N, mono- or polycyclic> / 25 / carbocycle <containing 3 or more C, non-aromatic, 0 or more double bonds, mono- or polycyclic> (opt. substd.) / aryl <containing 6 or more C, mono- or polycyclic> (opt. substd.) / heterocycle <containing 3 or more atoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, mono- or polycyclic> / heteroaryl <containing zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or polycyclic>



G2 = F / Cl / Br / I / CN / NO2 / OH / SH / 32 / 30 / 27 / 34 / 38 / heteroaryl <containing zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or polycyclic>



G49 = carbocycle <containing 5-6 C,
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G47) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G47) / 146

G48=O
146

Patent location: claim 1
Note: substitution is restricted
Note: additional interruptions in G14 and G32 also claimed
Note: and pharmaceutically acceptable salts and N-oxides
Stereochemistry: and isomers and racemic forms

L86 ANSWER 21 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 135:344472 MARPAT
TITLE: Preparation of 6-(5-oxazolyl)-4(1H)-quinolinones as inhibitors of IMPDH enzyme
INVENTOR(S): Iwanowicz, Edwin J.; Watterson, Scott H.; Dhar, T. G. Murali; Pitts, William J.; Gu, Henry H.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 263 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081340	A2	20011101	WO 2001-US12900	20010419
WO 2001081340	A3	20020523		
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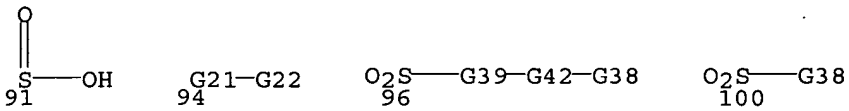
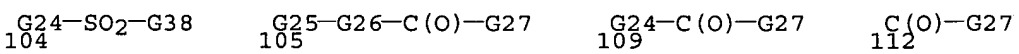
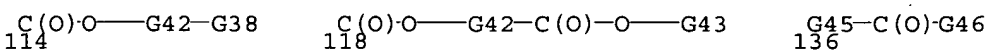
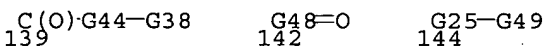
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2407370	AA	20011101	CA 2001-2407370	20010419
EP 1276739	A2	20030122	EP 2001-928708	20010419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003531205	T2	20031021	JP 2001-578430	20010419
US 2002040022	A1	20020404	US 2001-840503	20010423
US 6919335	B2	20050719		
PRIORITY APPLN. INFO.:			US 2000-199420P	20000424
			WO 2001-US12900	20010419

GI

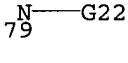




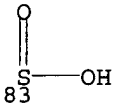




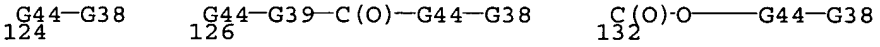
G38 = NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C>
G39 = NH / 79



G40 = H / alkyl <containing 1-6 C> / OH / alkoxy <containing 1-6 C>
G41 = 83 / alkylsulfonyl <containing 1-6 C>



G42 = (1-4) CH2
G43 = alkyl <containing 1-6 C> / 124 / 126 / 132



G44 = alkylene <containing 1-6 C>
G45 = cycloalkylene <containing 3-6 C>
G46 = OH / alkoxy <containing 1-6 C>
G47 = alkyl <containing 1-6 C> / F / Cl / Br / I / OH / CN / tetrazolyl / NH2 / CO2H / alkoxycarbonyl <containing 1-6 C>
G48 = carbocycle <containing 5-6 C, 5- to 6-membered monocyclic ring> (opt. substd.) / heterocycle <containing 5-6 atoms, 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 5- to 6-membered monocyclic ring> (opt. substd.)

G32—G36
66 67

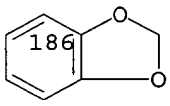
G32 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G33) / 69-9 71-67 /
(Specifically claimed: CH2)

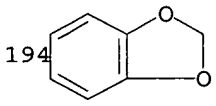
G34—G35—G34
69 71

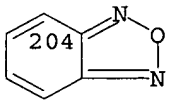
G33 = Ph / F / Cl / Br / I / NH2 / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / CO2H /
alkoxycarbonyl <containing 1-6 C>
G34 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G35 = O / S / S(O) / SO2 / NH / 72 / C(O)

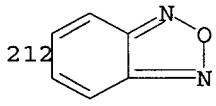
N——G10
72

G36 = carbocycle <containing 5-10 C, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G37) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms), mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G37) /
(Specifically claimed: Ph (opt. substd.) / pyridyl / 186 /
194 / 204 / 212)









G37 = alkyl <containing 1-6 C> / F / Cl / Br / I / CN /
NO2 / CF3 / OCF3 / NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / 74 / 76 / 81 /
86 / OH / 94 / SH / 89 / 91 / 96 / 100 / 104 / 105 / 109 /
112 / 114 / 118 / 136 / 139 / carbocycle <containing 5-6 C,
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G47) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G47) / 142 / 144

G24—G38
74

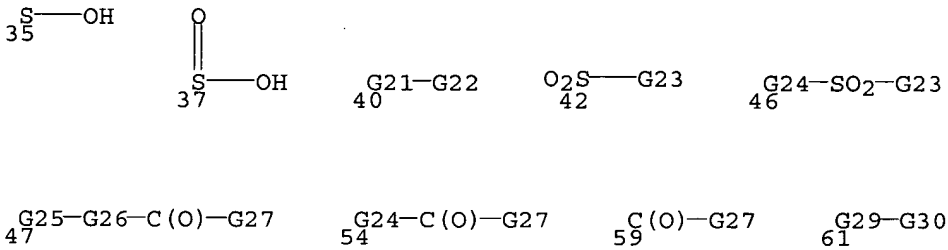
G39—C(O)-G40
76

G39—G41
81

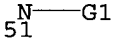
G41
|
N——G41
86

S——OH
89

37 / 40 / 42 / 46 / 47 / 54 / 59 /
carbocycle <containing 5-6 C, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G28) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G28) / 61



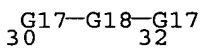
G21 = O / S / S(O) / SO2
G22 = alkyl <containing 1-6 C>
G23 = NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C>
G24 = (1-3) CH2
G25 = O / S / S(O) / SO2 / NH / 51



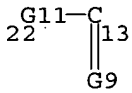
G26 = (0-3) CH2
G27 = OH / alkoxy <containing 1-6 C> / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C>
G28 = alkyl <containing 1-6 C> / F / Cl / Br / I / OH / NH2
G29 = CH2 / O / S / S(O) / SO2 / NH / 63

G30 = carbocycle <containing 5-6 C, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G28) / heterocycle <containing 5-6 atoms, 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G28)
G31 = H / alkyl <containing 1 or more C> (opt. substd.) / alkenyl <containing 3 or more C> (opt. substd.) / alkynyl <containing 3 or more C> (opt. substd.) / 66 / carbocycle <containing 5-10 C, mono- or bicyclic, 5- or 6-membered rings only> (opt. substd. by (1-7) G37) / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic, 5- or 6-membered rings only> (opt. substd. by (1-7) G37)

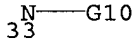
G12 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more aryl) / cycloalkyl / aryl /
heteroaryl <containing zero or more N, zero or more O,
zero or more S>
G13 = H / alkyl <containing 1-6 C>
(opt. substd. by 1 or more aryl) / aryl /
heterocycle <containing zero or more N, zero or more O,
zero or more S> / cycloalkyl
G14 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 30-28 32-29



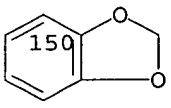
G15 = F / Cl / Br / I / NH2 / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / CO2H /
alkoxycarbonyl <containing 1-6 C>
G16 = 22-23 13-1 / **bond**

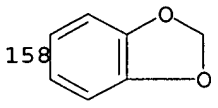


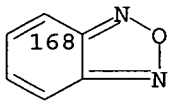
G17 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G18 = O / S / S(O) / SO2 / NH / 33

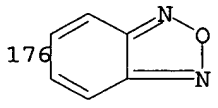


G19 = carbocycle <containing 5-10 C, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G20) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms), mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G20) /
(Specifically claimed: Ph (opt. substd.) / pyridyl / 150 /
158 / 168 / 176)

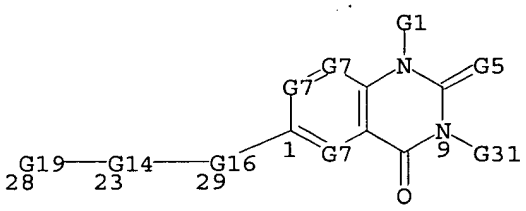








G20 = alkyl <containing 1-6 C> / F / Cl / Br / I / CN /
NO2 / SCF3 / CF3 / OCF3 / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / OH / SH / 35 /



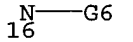
G1 = H / NH2 / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G2) /
alkenyl <containing 3-6 C> (opt. substd. by 1 or more G3) /
alkynyl <containing 3-6 C> (opt. substd. by 1 or more G3) /
aryl (opt. substd. by 1 or more G3) /
heterocycle <containing zero or more N, zero or more O,
zero or more S> (opt. substd. by 1 or more G3) /
(Specifically claimed: Me)

G2 = alkylamino <containing 1-6 C>
(opt. substd. by 1 or more G3) /
dialkylamino <each alkyl containing 1-6 C>
(opt. substd. by 1 or more G3) /
aryl (opt. substd. by 1 or more G3) /
cycloalkyl <containing 3-6 C> (opt. substd. by 1 or more G3)
/ NH2 / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G4) / CN / CO2H /
alkoxycarbonyl <containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C>

G3 = NH2 / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G4) / CN / CO2H /
alkoxycarbonyl <containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C>

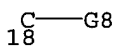
G4 = F / Cl / Br / I

G5 = O / S / **16**



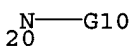
G6 = alkyl <containing 1-6 C> / OH / CN

G7 = **(up to 2) N / 18**



G8 = H / alkyl <containing 1-6 C> / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / **F** / Cl / Br / I

G9 = O / S / NH / 20



G10 = alkyl <containing 1-6 C>

G11 = O / S / NH / 24 / 26

	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
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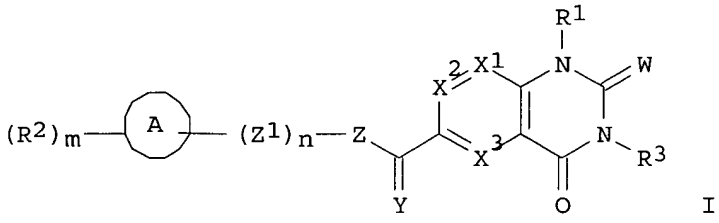
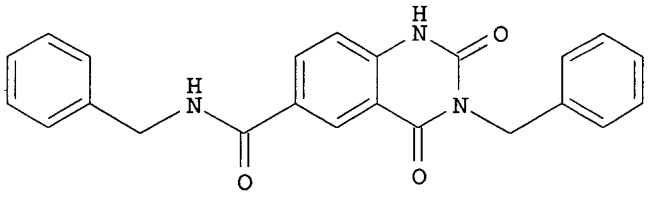
	JP 2004523546	T2	20040805	JP 2002-564505	20020211
	CN 1537105	A	20041013	CN 2002-805014	20020211
	BR 2002007268	A	20050315	BR 2002-7268	20020211
	US 2002193377	A1	20021219	US 2002-75954	20020213
	ZA 2003006008	A	20041104	ZA 2003-6008	20030804
	NO 2003003593	A	20030813	NO 2003-3593	20030813
	BG 108091	A	20041230	BG 2003-108091	20030813
PRIORITY APPLN. INFO.:				US 2001-268661P	20010214
				WO 2002-EP1979	20020211

OTHER SOURCE(S): CASREACT 137:185501

GI



I

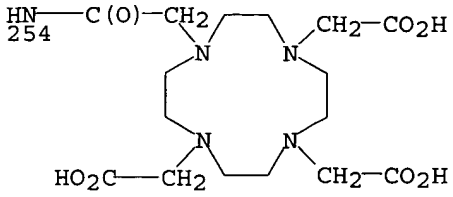


II

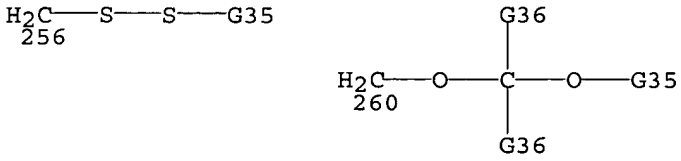
AB Title compds. I [R1 = H, amino, alkyl, alkenyl, alkynyl, alkylamino, aryl, heterocycle, etc.; W = O, S, =N-R'; R' = alkyl, OH, CN; X1-3 = N, C-R6; R6 = H, alkyl, amino, alkylamino, etc.; Y = O, S, NH, N-alkyl; Z = O, S, NR7; R7 = H, alkyl, aryl, aryl, heteroaryl, etc.; n = 1-8; Z1 = alkyl; A = (non)aromatic, 5- or 6-membered monocycle comprising from 0 to 4 heteroatoms selected from N, O, S, etc.; m = 0-7; R2 = alkyl, halo, CN, NO2, SCF3, CF3, OCF3, etc.; R3 = H, alkyl, alkenyl, alkynyl, etc.] were prepared Over 200 synthetic examples were provided. For instance, di-Me 4-aminoisophthalate was reacted with benzylisocyanate and heated to 95-100° overnight to give Me 3-benzyl-2,4-dioxo-1,2,3,4-tetrahydroquinazoline-6-carboxylate which was saponified (dioxaneaq, LiOH, reflux) to give the carboxylic acid. This intermediate was coupled with benzylamine to afford II. Selected examples of I had IC50 = 2.25 - 0.001 μM for MMP13 and IC50 > 100 μM for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12 and MMP14; II had IC50 = 0.193 μM for MMP13. Compds. I are useful for the treatment of osteoarthritis and rheumatoid arthritis.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1



G34 = H / 256 / 260

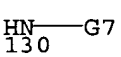


G35 = R <"drug or drug bearing moiety">
G36 = H / alkyl / cycloalkyl / Ph (substd.)
G37 = alkylene <containing 1-12 C>
Patent location: claim 1
Note: also incorporates claim 9
Note: substitution is restricted

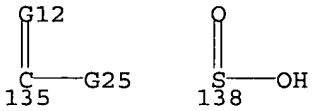
L86 ANSWER 20 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 137:185501 MARPAT
TITLE: Preparation of quinazolines as specific inhibitors of type-13 matrix metalloprotease
INVENTOR(S): Andrianjara, Charles; Chantel-Barvian, Nicole; Gaudilliere, Bernard; Jacobelli, Henri; Ortwine, Daniel Fred; Patt, William Chester; Pham, Ly; Kostlan, Catherine Rose; Wilson, Michael William
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 264 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064572	A1	20020822	WO 2002-EP1979	20020211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2437122	AA	20020822	CA 2002-2437122	20020211
EP 1368324	A1	20031210	EP 2002-722137	20020211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

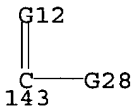
G25 = H / OH / 130



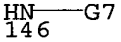
G26 = H / 135 / 138



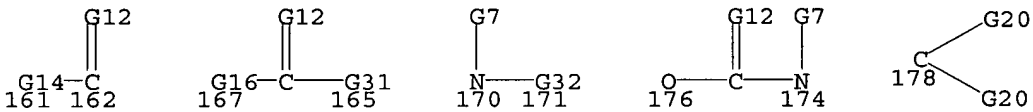
G27 = 143 / H

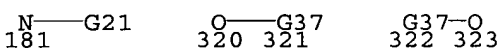


G28 = H / 146

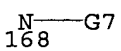


G29 = 161-7 162-160 / 167-7 165-160 / 170-7 171-160 / 176-7 174-160 / O / S / S(O) / SO2 / 178 / 181 / alkylene <containing 1-12 C> / 320-7 321-160 / 322-7 323-160

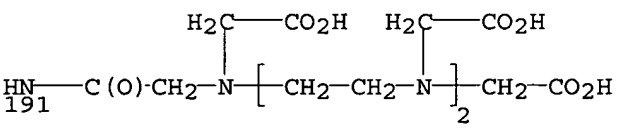




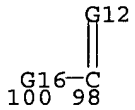
G30 = R <"leaving or linking group, or diagnostic or therapeutic agent">
G31 = O / 168



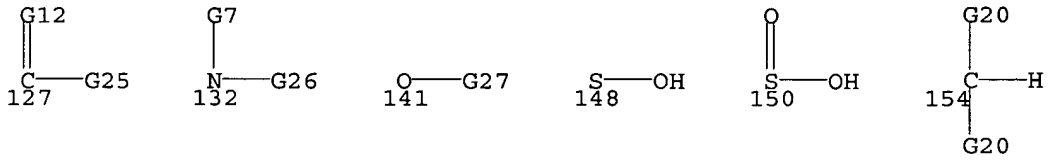
G32 = bond / SO2
G33 = 191 / 254

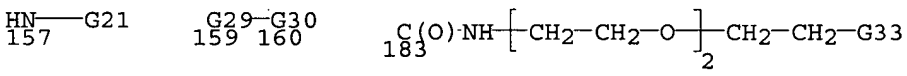


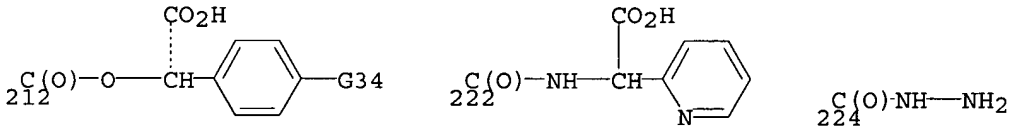
G20 = H / R / (Specifically claimed: Me)
G21 = ethynyl / propargyl
G22 = 100-3 98-96 / bond

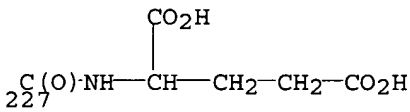


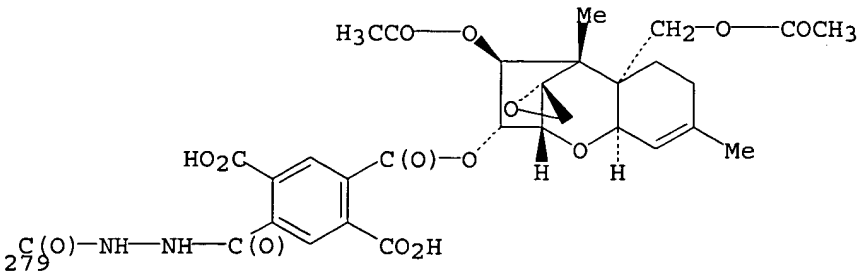
G23 = H / R <"leaving or linking group, or diagnostic or therapeutic agent"> / 127 / 132 / 141 / SH / 148 / 150 / 154 / 157 / alkyl <containing 1-12 C> (opt. substd. by OH) / alkoxy <containing 1-12 C> / 159 / (Examples: 183 / 212 / 222 / 224 / 227 / 279)



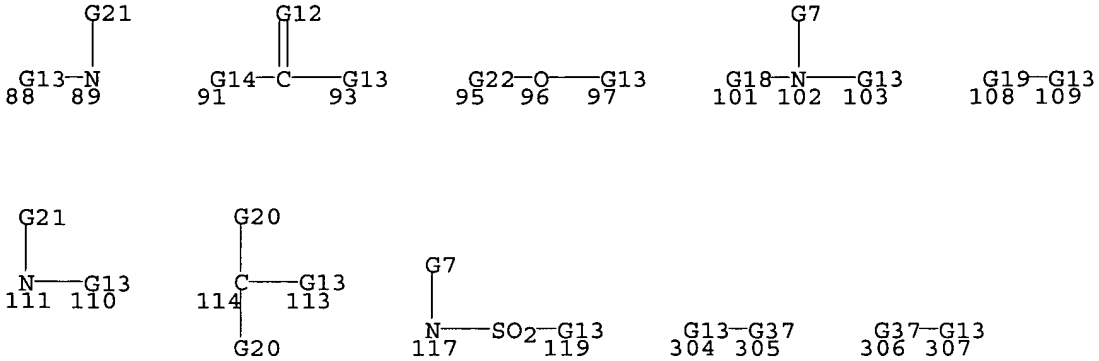




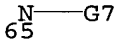




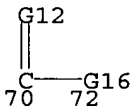
G24 = **CH / N**



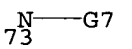
G12 = O / S
G13 = **CH2 (opt. substd.)** / C(O)
G14 = bond / **O** / 65



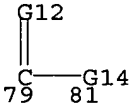
G15 = 70-68 72-7 / bond



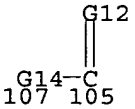
G16 = bond / 73



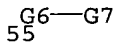
G17 = bond / 79-76 81-7 / SO2



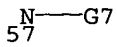
G18 = bond / 107-3 105-102



G19 = S / S(O) / SO2

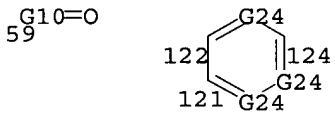


G6 = O / S / **57**



G7 = H / F / Cl / Br / I / At /
alkyl <containing 1-12 C> / alkoxy <containing 1-12 C> /
CHO / alkylcarbonyl <containing 1-11 C> /
alkenyl <containing 2-12 C> / alkynyl <containing 2-12 C> /
alkoxycarbonyl <containing 1-12 C> /
alkylaminocarbonyl <containing 1-12 C> /
dialkylaminocarbonyl <each alkyl containing 1-12 C> /
(Specifically claimed: Me)

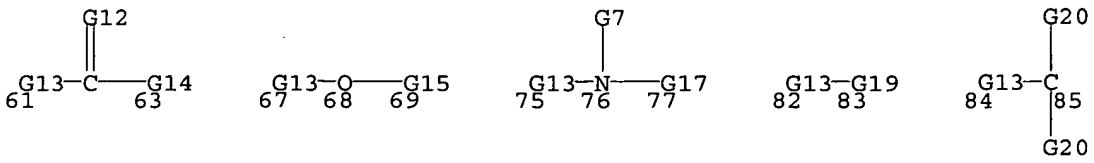
G8 = any ring <containing 0-3 heteroatoms,
0-3 N (no other heteroatoms), 3 or more C,
1 or more double bonds, attached through 3 or more C,
6-membered monocyclic ring> (opt. substd. by 1 or more G9) /
59 / **(Specifically claimed: 122-2 121-4 124-6)**



G9 = F / Cl / Br / I / At / alkyl <containing 1-12 C> /
alkoxy <containing 1-12 C> / CHO /
alkylcarbonyl <containing 1-11 C> /
alkenyl <containing 2-12 C> / alkynyl <containing 2-12 C> /
alkoxycarbonyl <containing 1-12 C> /
alkylaminocarbonyl <containing 1-12 C> /
dialkylaminocarbonyl <each alkyl containing 1-12 C>

G10 = any ring <containing 0-2 heteroatoms,
0-2 N (no other heteroatoms), 4 or more C,
1 or more double bonds, attached through 4 or more C,
6-membered monocyclic ring> (opt. substd.)

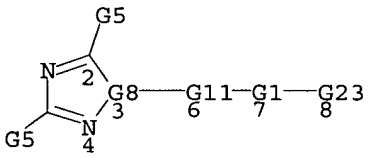
G11 = CH2 (opt. substd.) / C(O) / 61-3 63-7 /
67-3 69-7 / 75-3 77-7 / 82-3 83-7 / 84-3 85-7 /
88-3 89-7 / **91-3 93-7** / 95-3 97-7 / 101-3 103-7 /
108-3 109-7 / 111-3 110-7 / 114-3 113-7 / 117-3 119-7 /
304-3 305-7 / 306-3 307-7 / 308-3 310-7 / 311-3 313-7 /
314-3 316-7 / 317-3 319-7



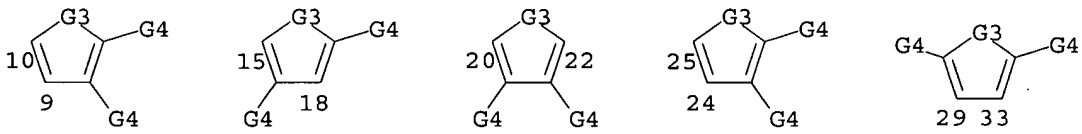
DMSO, followed by addition of DTPA tris(tert-butyl) ester. The folate mimetic is conjugated to a diagnostic or therapeutic agent to enable selective delivery of the agent to the targeted cell population. The 111In complex of II was selectively localized in the folate-receptor-pos. tumor xenografts of human KB cells in athymic mice (NuNu strain) and afforded prolonged tumor retention of 111In (5.4, 5.5, and 3.6% ID/g at 1 h, 4 h, and 24 h, resp.); blockable binding was also observed in the kidneys, where the folate receptor occurs in the proximal tubes.

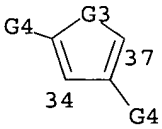
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1

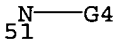


G1 = phenylene (opt. substd. by 1 or more G2) /
10-6 9-8 / 15-6 18-8 / 20-6 22-8 / 24-6 25-8 /
29-6 33-8 / 34-6 37-8





G2 = F / Cl / Br / I / At / alkyl <containing 1-12 C> /
alkoxy <containing 1-12 C> / (Specifically claimed: Me)
G3 = S / O / 51

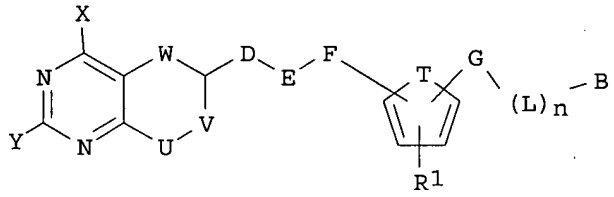


G4 = H / F / Cl / Br / I / At /
alkyl <containing 1-12 C> / alkoxy <containing 1-12 C> /
(Specifically claimed: Me)
G5 = F / Cl / Br / I / At / H /
alkyl <containing 1-12 C> / **alkoxy <containing 1-12 C>** /
CHO / alkylcarbonyl <containing 1-11 C> /
alkenyl <containing 2-12 C> / alkynyl <containing 2-12 C> /
alkoxycarbonyl <containing 1-12 C> /
alkylaminocarbonyl <containing 1-12 C> /
dialkylaminocarbonyl <each alkyl containing 1-12 C> / **55** /
(Specifically claimed: Me)

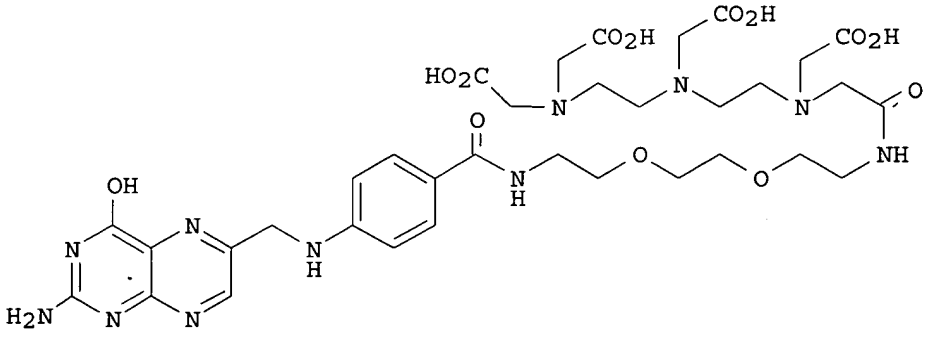
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1389209	A1	20040218	EP 2002-731495 20020424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 2004242582	A1	20041202	US 2004-475876 20040621
US 2005227985	A9	20051013	
PRIORITY APPLN. INFO.:			US 2001-286082P 20010424
			WO 2002-US13045 20020424

GI

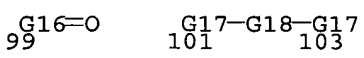


I

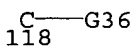


II

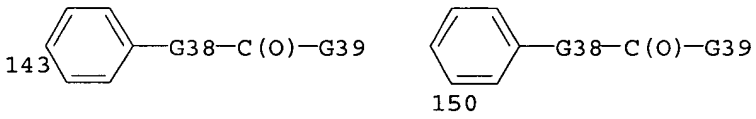
AB A cell population expressing folate receptors is selectively targeted with folate mimetic I [D = (CR6R7)s; E = (A1)p; F = (CR6R7)1-s; G = (A2)r; X, Y = halo, R2, OR2, SR3, NR4R5; U, V, W = (R6')C:, N:, (R6')C(R7'), N(R4'); T = S, O, N, C:C (such that T is part of an aromatic ring); A1, A2 = C(Z), C(Z)O, OC(Z), N(R4''), C(Z)N(R4''), N(R4'')C(Z), OC(Z)N(R4''), N(R4'')C(Z)O, N(R4'')C(Z)N(R5''), O, S, S(O), SO2, N(R4'')SO2, C(R6'')C(R7''), N(C.tplbond.CH), N(CH2C.tplbond.CH), C1-12-alkyl, C1-12-alkoxy; Z = O, S; R1 = H, halo, C1-12-alkyl, C1-12-alkoxy; R2 - R5, R4', R4'' - R7'' = H, halo, C1-12-alkyl, C1-12-alkoxy, C1-12-alkenyl, C1-12-alkynyl, (C1-12-alkoxy)carbonyl, (C1-12-alkylamino)carbonyl; R6, R7 = H, halo, C1-12-alkyl, C1-12-alkoxy; R6R7 = O; R6', R7' = H, halo, C1-12-alkyl, C1-12-alkoxy; R6'R7' = O; L = divalent linker (with the proviso that L ≠ naturally occurring amino acid covalently linked to A2 at its α-amino group through an amide bond); n, p, r, s = 0, 1; B = H, leaving group]. Thus, CYK4-013 (II) was prepared from pteroic acid via coupling with (CH2OCH2CH2NH2)2 using PyBOP, HOBt and N-methylmorpholine in

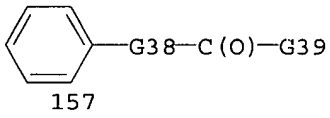


G35 = N / 118



G36 = H / R / (Specifically claimed: Me)
G37 = carbocycle <containing 5-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
(Specifically claimed: Ph / 143 / 150 / 157)



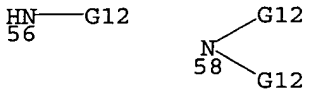


G38 = (0-3) CH2
G39 = OH / alkoxy <containing 1-6 C> /
(Specifically claimed: OMe)
Patent location: claim 21

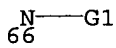
L86 ANSWER 19 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 137:338133 MARPAT
TITLE: Preparation of folate mimetics and folate-receptor binding conjugates thereof
INVENTOR(S): Green, Mark A.; Leamon, Christopher P.; Ke, Chun-Yen
PATENT ASSIGNEE(S): Purdue Research Foundation, USA; Endocyte, Inc.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085908	A1	20021031	WO 2002-US13045	20020424

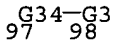
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,



G25 = O / S / NH / 66



G26 = OH / alkoxy <containing 1-6 C>
G27 = CH2 / O / S / S(O) / SO2
G28 = carbocycle <containing 5-6 C,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G29) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G29)
G29 = alkyl <containing 1-6 C> / halo /
alkyl <containing 1-6 C> (substd. by (3) halo) / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C>
G30 = aryl <containing up to 10 C>
(opt. substd. by 1 or more G4)
G31 = cycloalkyl <containing 3-10 C>
(opt. substd. by 1 or more G4)
G32 = H / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G33) /
alkenyl <containing 3-6 C> (opt. substd. by 1 or more G33) /
alkynyl <containing 3-6 C> (opt. substd. by 1 or more G33) /
97 / carbocycle <containing 5-10 C, 0 or more double bonds,
mono- or bicyclic, 5- or 6-membered rings only>
(opt. substd. by (1-7) G21) / heterocycle <containing 5-10
atoms, 1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21)



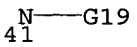
G33 = NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> /
alkyl <containing 1-6 C> (opt. substd. by (3) halo) / CN /
CO2H / alkoxycarbonyl <containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>
G34 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 99 / 101-20 103-98 /
(Specifically claimed: CH2)

G15 = halo / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C> / OH / SH / alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C> / CO2H / alkoxycarbonyl <containing 1-6 C>

G16 = carbon chain <containing 1 or more C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)

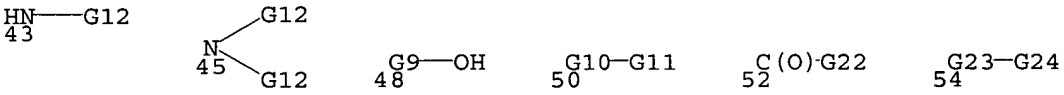
G17 = carbon chain <containing 1 or more C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)

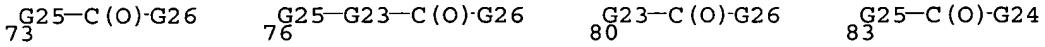
G18 = O / S / S(O) / SO2 / NH / 41

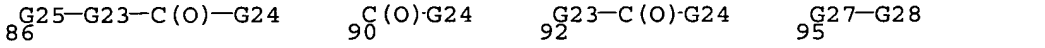


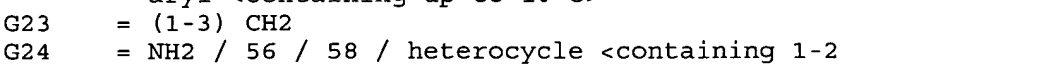
G19 = alkyl <containing 1-6 C>

G21 = alkyl <containing 1-6 C> / halo / CN / NO2 / alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 43 / 45 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring> / OH / SH / 48 / 50 / 52 / 54 / 61 / 63 / 68 / 71 / 73 / 76 / CO2H / alkoxycarbonyl <containing 1-6 C> / 80 / 83 / 86 / 90 / 92 / 95 / carbocycle <containing 5-6 C, 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G29) / heterocycle <containing 5-6 atoms, 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G29)









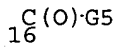
G22 = alkyl <containing 1-6 C> / aryl <containing up to 10 C>

G23 = (1-3) CH2

G24 = NH2 / 56 / 58 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>

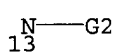
zero or more O, zero or more S (no other heteroatoms), monocyclic> (opt. substd. by 1 or more G4) / heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G4) / (Specifically claimed: Me)

G4 = halo / NH2 / alkylamino <containing 1-10 C> / dialkylamino <each alkyl containing 1-10 C> / CN / alkyl <containing 1-6 C> (substd. by (3) halo) / 16 / OH / SH / alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>

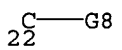


G5 = alkyl <containing 1-6 C> / aryl <containing up to 10 C> / OH / alkoxy <containing 1-16 C>

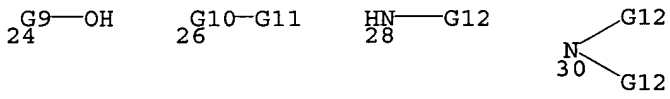
G6 = O / S / **NH** / 13



G7 = **(up to 2) N / 22**



G8 = H / alkyl <containing 1-6 C> / OH / alkoxy <containing 1-6 C> / **halo** / CF3 / CN / NO2 / SH / 24 / 26 / NH2 / 28 / 30 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>



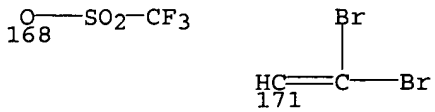
G9 = S / S(O)

G10 = S / S(O) / SO2

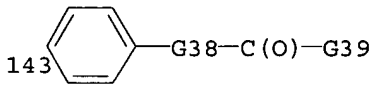
G11 = alkyl <containing 1-6 C>

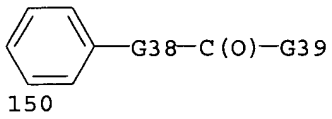
G12 = alkyl <containing 1-6 C> / alkyl <containing 1-10 C> (substd. by 1 or more aryl <containing up to 10 C>)

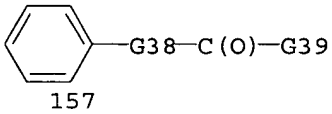
G13 = H / halo / OSO2Me / 168 / CHO / COMe / R <"ester group"> / ethynyl / 171 / (Specifically claimed: I)



5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
(Specifically claimed: Ph / 143 / 150 / 157)

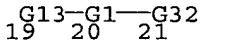




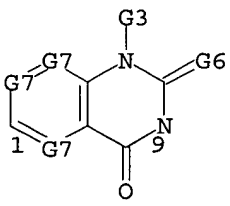


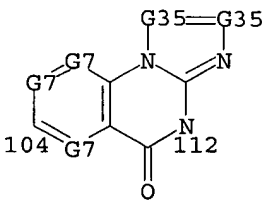
G38 = (0-3) CH2
G39 = OH / alkoxy <containing 1-6 C> /
(Specifically claimed: OMe)
Patent location: claim 1
Note: and N-oxides or pharmaceutically acceptable acid or base addition salts
Note: additional heteroatom interruptions in G17 also claimed
Stereochemistry: and optical isomers

MSTR 2



G1 = **1-19 9-21** / 104-19 112-21





G2 = alkyl <containing 1-6 C> / OH / CN
G3 = H / CF3 / NH2 / alkylamino <containing 1-10 C> /
dialkylamino <each alkyl containing 1-10 C> /
alkyl <containing 1-6 C> (opt. substd. by 1 or more G4) /
alkenyl <containing 3-6 C> (opt. substd. by 1 or more G4) /
alkynyl <containing 3-6 C> (opt. substd. by 1 or more G4) /
aryl <containing up to 10 C> (opt. substd. by 1 or more G4) /
alkyl <containing 1-10 C> (substd. by 1 or more G30) /
alkyl <containing 1-10 C> (substd. by G31) /
heteroaryl <containing 1-4 heteroatoms, zero or more N,

G26 = OH / alkoxy <containing 1-6 C>
G27 = CH2 / O / S / S(O) / SO2
G28 = carbocycle <containing 5-6 C,
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G29) /
heterocycle <containing 5-6 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, 5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G29)
G29 = alkyl <containing 1-6 C> / halo /
alkyl <containing 1-6 C> (substd. by (3) halo) / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C>
G30 = aryl <containing up to 10 C>
(opt. substd. by 1 or more G4)
G31 = cycloalkyl <containing 3-10 C>
(opt. substd. by 1 or more G4)
G32 = H / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G33) /
alkenyl <containing 3-6 C> (opt. substd. by 1 or more G33) /
alkynyl <containing 3-6 C> (opt. substd. by 1 or more G33) /
97 / carbocycle <containing 5-10 C, 0 or more double bonds,
mono- or bicyclic, 5- or 6-membered rings only>
(opt. substd. by (1-7) G21) / heterocycle <containing 5-10
atoms, 1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21)

G34—G37
97 98

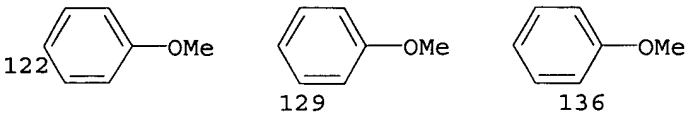
G33 = NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> /
alkyl <containing 1-6 C> (opt. substd. by (3) halo) / CN /
CO2H / alkoxycarbonyl <containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>
G34 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 99 / 101-20 103-98 /
(Specifically claimed: CH2)

G16=O G17—G18—G17
99 101 103

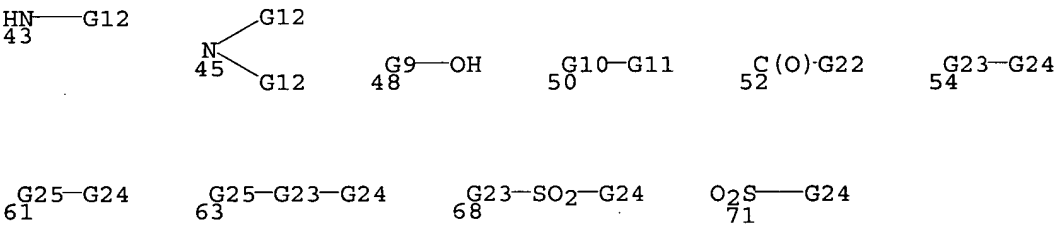
G35 = N / 118

C——G36
118

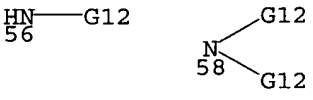
G36 = H / R / (Specifically claimed: Me)
G37 = carbocycle <containing 5-10 C,
0 or more double bonds, mono- or bicyclic,



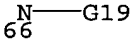
G21 = alkyl <containing 1-6 C> / halo / CN / NO2 / alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 43 / 45 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring> / OH / SH / 48 / 50 / 52 / 54 / 61 / 63 / 68 / 71 / 73 / 76 / CO2H / alkoxycarbonyl <containing 1-6 C> / 80 / 83 / 86 / 90 / 92 / 95 / carbocycle <containing 5-6 C, 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G29) / heterocycle <containing 5-6 atoms, 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G29)



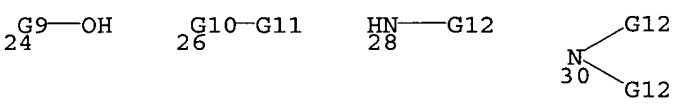
G22 = alkyl <containing 1-6 C> / aryl <containing up to 10 C>
G23 = (1-3) CH2
G24 = NH2 / 56 / 58 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>



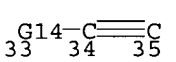
G25 = O / S / NH / 66



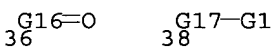
alkoxy <containing 1-6 C> / **halo** / CF3 / CN / NO2 / SH / 24 /
26 / NH2 / 28 / 30 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>



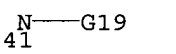
G9 = S / S(O)
G10 = S / S(O) / SO2
G11 = alkyl <containing 1-6 C>
G12 = alkyl <containing 1-6 C> / alkyl <containing 1-10 C> (substd. by 1 or more aryl <containing up to 10 C>)
G13 = ethynylene / 33-18 35-20



G14 = carbon chain <containing 1 or more C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by 1 or more G15) / 36 / 38-18 40-34 / (Specifically claimed: CH2)



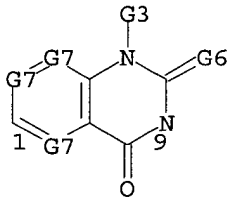
G15 = halo / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C> / OH / SH / alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C> / CO2H / alkoxycarbonyl <containing 1-6 C>
G16 = carbon chain <containing 1 or more C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)
G17 = carbon chain <containing 1 or more C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)
G18 = O / S / S(O) / SO2 / NH / 41

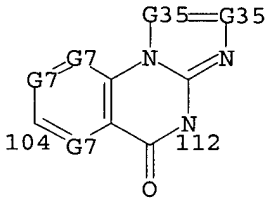


G19 = alkyl <containing 1-6 C>
G20 = carbocycle <containing 5-10 C, 0 or more double bonds, mono- or bicyclic, 5- or 6-membered rings only> (opt. substd. by (1-7) G21) / heterocycle <containing 5-10 atoms, 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 5- or 6-membered rings only> (opt. substd. by (1-7) G21) / (Specifically claimed: Ph / 122 / 129 / 136)

G20—G13—G1—G32
18 19 20 21

G1 = **1-19 9-21** / 104-19 112-21





G2 = alkyl <containing 1-6 C> / OH / CN
G3 = H / CF3 / NH2 / alkylamino <containing 1-10 C> /
dialkylamino <each alkyl containing 1-10 C> /
alkyl <containing 1-6 C> (opt. substd. by 1 or more G4) /
alkenyl <containing 3-6 C> (opt. substd. by 1 or more G4) /
alkynyl <containing 3-6 C> (opt. substd. by 1 or more G4) /
aryl <containing up to 10 C> (opt. substd. by 1 or more G4) /
alkyl <containing 1-10 C> (substd. by 1 or more G30) /
alkyl <containing 1-10 C> (substd. by G31) /
heteroaryl <containing 1-4 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
monocyclic> (opt. substd. by 1 or more G4) /
heterocycle <containing 1-4 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
non-aromatic, 0 or more double bonds,
5- to 6-membered monocyclic ring>
(opt. substd. by 1 or more G4) / (Specifically claimed: Me)
G4 = halo / NH2 / alkylamino <containing 1-10 C> /
dialkylamino <each alkyl containing 1-10 C> / CN /
alkyl <containing 1-6 C> (substd. by (3) halo) / 16 / OH /
SH / alkoxy <containing 1-6 C> /
alkylthio <containing 1-6 C>

C(O)-G5
16

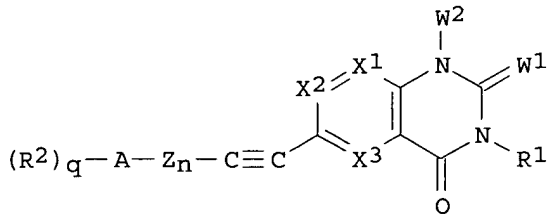
G5 = alkyl <containing 1-6 C> /
aryl <containing up to 10 C> / OH /
alkoxy <containing 1-16 C>
G6 = O / S / **NH** / 13

N——G2
13

G7 = **(up to 2) N / 22**

C——G8
22

G8 = H / alkyl <containing 1-6 C> / OH /



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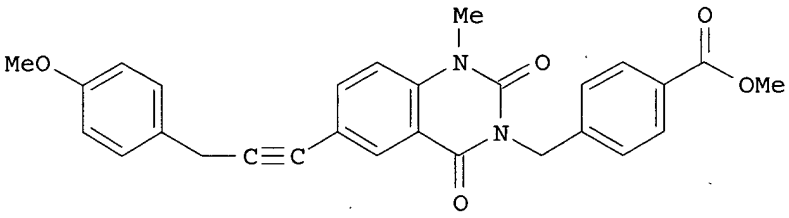

II

AB Title compds. I [wherein A = (hetero)aryl or (hetero)cycloalkyl; W1 = O, S, or NR3; W2 = H, CF3, NH2, (di)alkylamino, or (un)substituted (cycloalkyl)alkyl, alkenyl, (hetero)aryl, arylalkyl, or heterocyclylalkyl; or W1W2 = NX4=W3; W3 = N or CR5; X1-X3 = independently N or (un)substituted C; X4 = N or CR7; X5 = O, S, NH, or N-alkyl; X6 = bond, CH2, O, SO0-2; Z = CR12R13; R1 = H, alkyl, alkenyl, alkynyl, or (un)substituted (hetero)aryl or (hetero)cycloalkyl; R2 = independently H, (trihalo)alkyl, halo, CN, NO2, (CH2)kNR10R11, OR14, SR14, SOR14, SO2R14, acyl, X5(CH2)kNR10R11 (CH2)kSO2NR14R15, X5(CH2)kCO2R14, (CH2)kCO2R14, X5(CH2)kCONR14R15, (CH2)kCONR14R15 X6R16, and trialkylsiloxy; R3 = H, alkyl, OH, or CN; R4 = H or alkyl; R5 = H, OR6, SR6, or (un)substituted (cyclo)alkyl, (hetero)aryl, arylalkyl, or heterocyclylalkyl; R6, R8, and R9 = independently H or (aryl)alkyl; R7 = H, NR8R9, OR8, SR8, or (un)substituted (cyclo)alkyl, (hetero)aryl, arylalkyl, or heterocyclylalkyl; R10 and R11 = independently H, (hydroxy)alkyl, or arylalkyl; or NR10R11 = (un)substituted heterocyclyl; R12 and R13 = independently H, (trihalo)alkyl, halo, NH2, (di)alkylamino, OR4, SR4, or CO2R4; R14 and R15 = independently H or alkyl; R16 = (un)substituted (hetero)aryl or (hetero)cycloalkyl; k = 0-3; n = 0-8; q = 0-7; with provisos; or isomers, N-oxides, or pharmaceutically acceptable salts thereof] were prepared as specific inhibitors of type 13 matrix metalloprotease (MMP-13). For example, reaction of Me 4-(aminomethyl)benzoate•HCl with 2-amino-5-iodobenzoic acid using DEC•HCl and TEA in DMF provided the amide (70%). Cyclization using 1,1'-carbonyldiimidazole in THF gave the quinazoline (99.5%), which was methylated using MeI in the presence of K2CO3 in DMF to afford Me 4-(6-iodo-1-methyl-2,44-dioxo-1,4-dihydro-2H-quinazolin-3-ylmethyl)benzoate (64.2%). Substitution with 3-(4-methoxyphenyl)prop-1-yne catalyzed by Pd(PPh3)2Cl2 and CuI in TEA gave II (6%). Invention compds. inhibited the proteolysis of a peptide substrate with MMP-13 with IC50 values <1 μM, generally 100 times lower than the IC50 values for the same compds. with respect to MMP-1, MMP-2, MMP-3, MMP-7, MMP-9, MMP-12, and MMP-14. Thus, I are useful for the treatment of arthritis, cancer, and other diseases mediated by MMP-13 (no data).

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1

INVENTOR(S): Gaudilliere, Bernard; Jacobelli, Henry
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033477	A1	20030424	WO 2001-EP11824	20011012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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CA 2463159	AA	20030424	CA 2002-2463159	20021011
WO 2003033478	A1	20030424	WO 2002-EP12194	20021011
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US 2003130278	A1	20030710	US 2002-269197	20021011
US 6962922	B2	20051108		
BR 2002013239	A	20040928	BR 2002-13239	20021011
EP 1465878	A1	20041013	EP 2002-801341	20021011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005509626	T2	20050414	JP 2003-536218	20021011
US 2005245548	A1	20051103	US 2005-148880	20050609
PRIORITY APPLN. INFO.:			US 2001-329181P	20011012
			WO 2001-EP11824	20011012
			US 2002-395441P	20020712
			WO 2002-EP8475	20020712
			US 2002-269197	20021011
			WO 2002-EP12194	20021011

GI

G17 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G18 = O / S / S(O) / SO2 / NH / 41

N—G19
41

G19 = alkyl <containing 1-6 C>
G30 = aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4)
G31 = carbocycle <containing 3-10 C, non-aromatic,
0 or more double bonds, mono- or bicyclic>
(opt. substd. by 1 or more G4)
G32 = H / alkyl <containing 1-6 C> (opt. substd.) /
alkenyl <containing 2-6 C> (opt. substd.) /
alkynyl <containing 2-6 C> (opt. substd.) / 97 /
carbocycle <containing 5-10 C, 0 or more double bonds,
mono- or bicyclic, 5- or 6-membered rings only>
(opt. substd.) / heterocycle <containing 5-10 atoms,
1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd.)

G34—G37
97 98

G34 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 99 / 101-20 103-98

G16=O G17—G18—G17
99 101 103

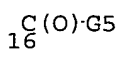
G35 = N / 118

C—G36
118

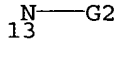
G36 = H / R
G37 = carbocycle <containing 5-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd.) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd.)
Patent location: claim 24

L86 ANSWER 18 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 138:338159 MARPAT
TITLE: Preparation of alkynylated fused ring pyrimidine
compounds as matrix metalloprotease 13 inhibitors

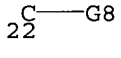
dialkylamino <each alkyl containing 1-6 C> / CN /
alkyl <containing 1-6 C> (substd. by (3) halo) / 16 / OH /
SH / alkoxy <containing 1-6 C> /
alkylthio <containing 1-6 C>



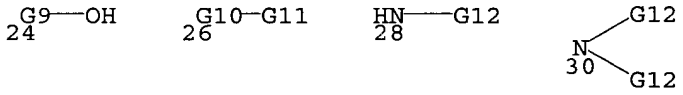
G5 = alkyl <containing 1-6 C> / Ph / OH /
alkoxy <containing 1-16 C>
G6 = O / S / **NH** / 13



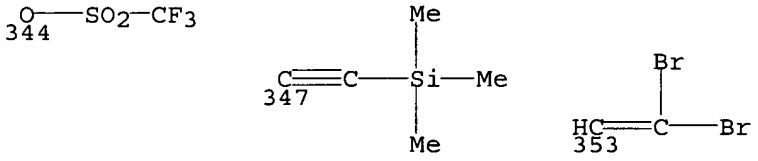
G7 = **(up to 2) N / 22**



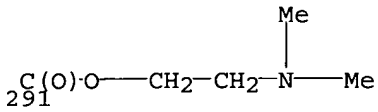
G8 = H / alkyl <containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / **halo** / CF3 / CN / NO2 / SH / 24
/
26 / NH2 / 28 / 30 / heterocycle <containing 1-2
heteroatoms, 1 or more N, zero or more O (no other
heteroatoms), attached through 1 or more N,
5- to 6-membered monocyclic ring>

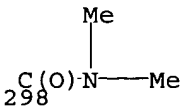


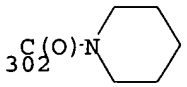
G9 = S / S(O)
G10 = S / S(O) / SO2
G11 = alkyl <containing 1-6 C>
G12 = alkyl <containing 1-6 C> /
alkyl <containing 1-6 C> (substd. by 1 or more aryl
<containing up to 10 C, mono- or bicyclic>)
G13 = H / halo / OSO2Me / 344 / CHO / COMe /
R <"ester group"> / 347 / ethynyl / 353

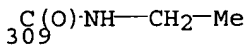


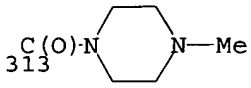
G15 = halo / NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C> /
CO2H / alkoxycarbonyl <containing 1-6 C>
G16 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)

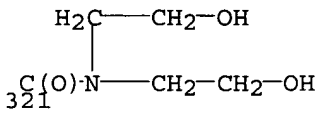






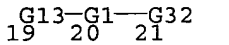




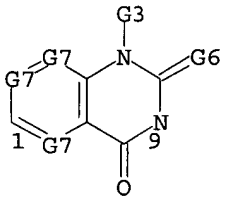


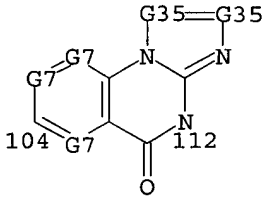
G50 = Cl / F
Patent location: claim 1
Note: and N-oxides or pharmaceutically acceptable acid or base addition salts
Note: additional heteroatom interruptions in G17 also claimed
Note: substitution is restricted
Stereochemistry: and optical isomers

MSTR 2

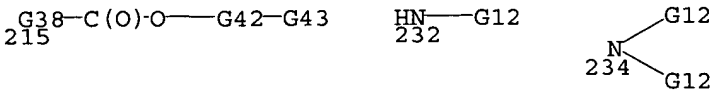


G1 = **1-19 9-21** / 104-19 112-21

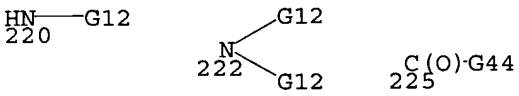




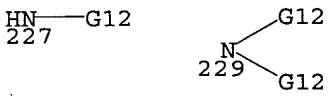
G2 = alkyl <containing 1-6 C> / OH / CN
G3 = H / CF3 / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C> / alkyl <containing 1-6 C> (opt. substd. by 1 or more G4) / alkenyl <containing 2-6 C> (opt. substd. by 1 or more G4) / alkynyl <containing 2-6 C> (opt. substd. by 1 or more G4) / aryl <containing up to 10 C, mono- or bicyclic> (opt. substd. by 1 or more G4) / alkyl <containing 1-6 C> (substd. by 1 or more G30) / alkyl <containing 1-6 C> (substd. by G31) / heteroaryl <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), monocyclic> (opt. substd. by 1 or more G4) / heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G4)
G4 = halo / NH2 / alkylamino <containing 1-6 C> /



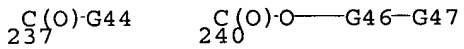
G42 = alkylene <containing 1-6 C>
G43 = OH / alkoxy <containing 1-6 C> / NH2 / 220 / 222 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring> / 225



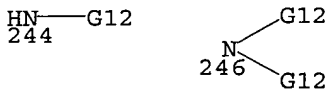
G44 = OH / alkoxy <containing 1-6 C> / NH2 / 227 / 229 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>



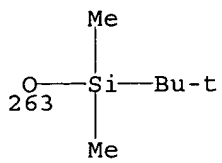
G45 = 237 / OH / alkoxy <containing 1-6 C> / 240 / (Specifically claimed: CO2Me)



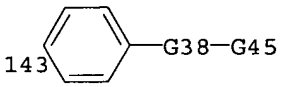
G46 = alkylene <containing 2-4 C>
G47 = NH2 / 244 / 246 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>

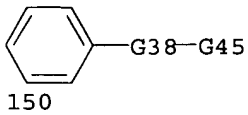


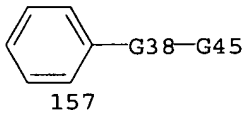
G48 = Ph / F / 263 / Cl

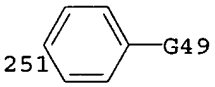


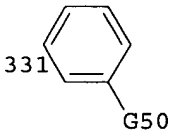
G49 = F / Cl / Br / CO2Bu-t / 291 / 298 / 302 / 309 / CH2OH / 313 / 321

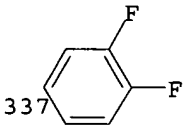












G38 = (0-3) CH2
G40 = alkyl <containing 1-6 C>
G41 = alkyl <containing 1-6 C> / halo / CN / NO2 /
alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 232 /
234 / heterocycle <containing 1-2 heteroatoms, 1 or more N,
zero or more O (no other heteroatoms),
attached through 1 or more N, 5- to 6-membered monocyclic
ring> / OH / SH / 173 / 175 / 177 / 179 / 181 / 183 / 186 /
189 / 191 / 194 / CO2H / alkoxycarbonyl <containing 1-6 C> /
198 / 201 / 204 / 208 / 210 / 213 / 215 /
aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by (1-4) G29) / heteroaryl <containing 1-4
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), mono- or bicyclic>
(opt. substd. by (1-4) G29) / heterocycle <containing 1-4
heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms), non-aromatic,
0 or more double bonds, mono- or bicyclic,
(1) 5- or more membered ring, (1) up to 6-membered ring>
(opt. substd. by (1-4) G29) / carbocycle <containing 3-10 C,
non-aromatic, 0 or more double bonds, mono- or bicyclic>
(opt. substd. by 1 or more G29)

173 G9—OH 175 G10—G11 177 C(O)-G22 179 G23—G24 181 G25—G24

183 G25—G23—G24 186 G23—SO2—G24 189 O2S——G24 191 G25—C(O)-G26

194 G25—G23—C(O)-G26 198 G23—C(O)-G26 201 G25—C(O)-G24

204 G25—G23—C(O)—G24 208 C(O)-G24 210 G23—C(O)-G24 213 G27—G28

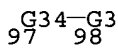
non-aromatic, 0 or more double bonds, mono- or bicyclic>
(opt. substd. by 1 or more G29)

G29 = alkyl <containing 1-6 C> / halo /
alkyl <containing 1-6 C> (substd. by (3) halo) / OH /
alkoxy <containing 1-6 C> / SH /
alkylthio <containing 1-6 C> / NH2 /
alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C>

G30 = aryl <containing up to 10 C, mono- or bicyclic>
(opt. substd. by 1 or more G4)

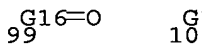
G31 = carbocycle <containing 3-10 C, non-aromatic,
0 or more double bonds, mono- or bicyclic>
(opt. substd. by 1 or more G4)

G32 = H / alkyl <containing 1-6 C>
(opt. substd. by 1 or more G33) /
alkenyl <containing 2-6 C> (opt. substd. by 1 or more G33) /
alkynyl <containing 2-6 C> (opt. substd. by 1 or more G33) /
97 / carbocycle <containing 5-10 C, 0 or more double bonds,
mono- or bicyclic, 5- or 6-membered rings only>
(opt. substd. by (1-7) G41) / heterocycle <containing 5-10
atoms, 1-4 heteroatoms, zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41)

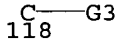


G33 = NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> /
alkyl <containing 1-6 C> (opt. substd. by (3) halo) / CN /
CO2H / alkoxycarbonyl <containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C>

G34 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 99 / 101-20 103-98 /
(Specifically claimed: CH2)

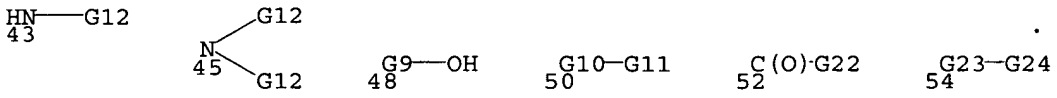


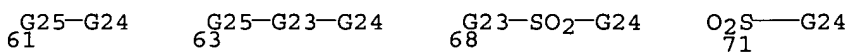
G35 = N / 118

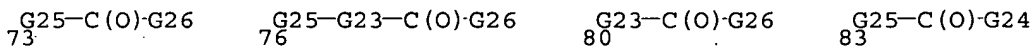


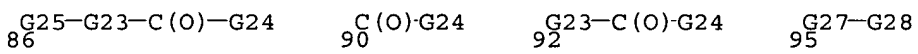
G36 = H / R / (Specifically claimed: Me)

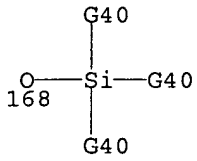
G37 = carbocycle <containing 5-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41) /
heterocycle <containing 5-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G41) /
(Specifically claimed: Ph / 143 / 150 / 157 / 251 / 331 /
337)



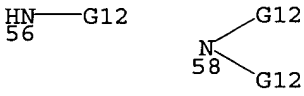




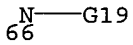




G22 = alkyl <containing 1-6 C> / Ph
G23 = (1-3) CH2
G24 = NH2 / 56 / 58 / heterocycle <containing 1-2 heteroatoms, 1 or more N, zero or more O (no other heteroatoms), attached through 1 or more N, 5- to 6-membered monocyclic ring>

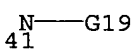


G25 = O / S / NH / 66

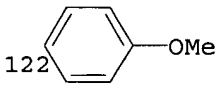


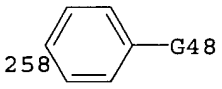
G26 = OH / alkoxy <containing 1-6 C>
G27 = CH2 / O / S / S(O) / SO2
G28 = aryl <containing up to 10 C, mono- or bicyclic> (opt. substd. by (1-4) G29) / heteroaryl <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), mono- or bicyclic> (opt. substd. by (1-4) G29) / heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, mono- or bicyclic, (1) 5- or more membered ring, (1) up to 6-membered ring> (opt. substd. by (1-4) G29) / carbocycle <containing 3-10 C,

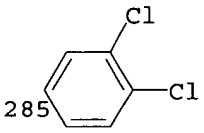
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G17 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)
G18 = O / S / S(O) / SO2 / NH / 41



G19 = alkyl <containing 1-6 C>
G20 = carbocycle <containing 8-10 C,
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
heterocycle <containing 8-10 atoms, 1-4 heteroatoms,
zero or more N, zero or more O,
zero or more S (no other heteroatoms),
0 or more double bonds, mono- or bicyclic,
5- or 6-membered rings only> (opt. substd. by (1-7) G21) /
(Specifically claimed: Ph / 122 / 258 / 270 / 275 / 280 /
285)

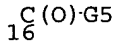




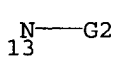


G21 = alkyl <containing 1-6 C> / halo / CN / NO2 /
alkyl <containing 1-6 C> (substd. by (3) halo) / NH2 / 43 /
45 / heterocycle <containing 1-2 heteroatoms, 1 or more N,
zero or more O (no other heteroatoms),
attached through 1 or more N, 5- to 6-membered monocyclic
ring> / OH / SH / 48 / 50 / 52 / 54 / 61 / 63 / 68 / 71 /
73 / 76 / CO2H / alkoxycarbonyl <containing 1-6 C> / 80 /
83 / 86 / 90 / 92 / 95 / aryl <containing up to 10 C,
mono- or bicyclic> (opt. substd. by (1-4) G29) /
heteroaryl <containing 1-4 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
mono- or bicyclic> (opt. substd. by (1-4) G29) /
heterocycle <containing 1-4 heteroatoms, zero or more N,
zero or more O, zero or more S (no other heteroatoms),
non-aromatic, 0 or more double bonds, mono- or bicyclic,
(1) 5- or more membered ring, (1) up to 6-membered ring>
(opt. substd. by (1-4) G29) / carbocycle <containing 3-10 C,
non-aromatic, 0 or more double bonds, mono- or bicyclic>
(opt. substd. by 1 or more G29) / 168

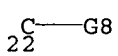
SH / alkoxy <containing 1-6 C> /
alkylthio <containing 1-6 C>



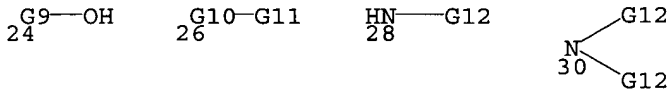
G5 = alkyl <containing 1-6 C> / Ph / OH /
alkoxy <containing 1-16 C>
G6 = O / S / **NH** / 13



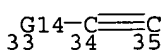
G7 = **(up to 2) N / 22**



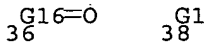
G8 = H / alkyl <containing 1-6 C> / OH /
alkoxy <containing 1-6 C> / **halo** / CF3 / CN / NO2 / SH / 24
/
26 / NH2 / 28 / 30 / heterocycle <containing 1-2
heteroatoms, 1 or more N, zero or more O (no other
heteroatoms), attached through 1 or more N,
5- to 6-membered monocyclic ring>



G9 = S / S(O)
G10 = S / S(O) / SO2
G11 = alkyl <containing 1-6 C>
G12 = alkyl <containing 1-6 C> /
alkyl <containing 1-6 C> (substd. by 1 or more aryl
<containing up to 10 C, mono- or bicyclic>)
G13 = ethynylene / 33-18 35-20



G14 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd. by 1 or more G15) / 36 / 38-18 40-34 /
(Specifically claimed: CH2 / C(O))

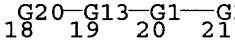


G15 = halo / NH2 / alkylamino <containing 1-6 C> /
dialkylamino <each alkyl containing 1-6 C> / OH / SH /
alkoxy <containing 1-6 C> / alkylthio <containing 1-6 C> /
CO2H / alkoxycarbonyl <containing 1-6 C>
G16 = carbon chain <containing 1 or more C,

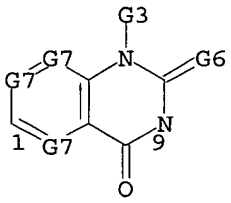
(trihalo)alkyl, halo, NH2, (di)alkylamino, OR4, SR4, or CO2R4; R14 and R15 = independently H or alkyl; R16 = (un)substituted (hetero)aryl or (hetero)cycloalkyl; k = 0-3; n = 0-8; q = 0-7; with provisos; or isomers, N-oxides, or pharmaceutically acceptable salts thereof] were prepared as specific inhibitors of type 13 matrix metalloprotease (MMP-13). For example, reaction of Me 4-(aminomethyl)benzoate•HCl with 2-amino-5-iodobenzoic acid using DEC•HCl and TEA in DMF provided the amide (70%). Cyclization using 1,1'-carbonyldiimidazole in THF gave the quinazoline (99.5%), which was methylated using MeI in the presence of K2CO3 in DMF to afford Me 4-(6-iodo-1-methyl-2,44-dioxo-1,4-dihydro-2H-quinazolin-3-ylmethyl)benzoate (64.2%). Substitution with 3-(4-methoxyphenyl)prop-1-yne catalyzed by Pd(PPh3)2Cl2 and CuI in TEA gave II (6%). Invention compds. inhibited the proteolysis of a peptide substrate with MMP-13 with IC50 values <10 μM, generally 100 times lower than the IC50 values for the same compds. with respect to MMP-1, MMP-2, MMP-3, MMP-7, MMP-9, MMP-12, and MMP-14. Thus, I are useful for the treatment of arthritis, cancer, and other diseases mediated by MMP-13 (no data).

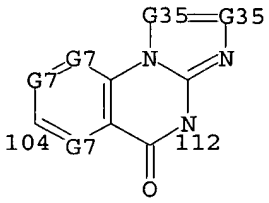
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1



G1 = **1-19 9-21** / 104-19 112-21





G2 = alkyl <containing 1-6 C> / OH / CN

G3 = H / CF3 / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C> / alkyl <containing 1-6 C> (opt. substd. by 1 or more G4) / alkenyl <containing 2-6 C> (opt. substd. by 1 or more G4) / alkynyl <containing 2-6 C> (opt. substd. by 1 or more G4) / aryl <containing up to 10 C, mono- or bicyclic> (opt. substd. by 1 or more G4) / alkyl <containing 1-6 C> (substd. by 1 or more G30) / alkyl <containing 1-6 C> (substd. by G31) / heteroaryl <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), monocyclic> (opt. substd. by 1 or more G4) / heterocycle <containing 1-4 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), non-aromatic, 0 or more double bonds, 5- to 6-membered monocyclic ring> (opt. substd. by 1 or more G4) / (Specifically claimed: Me)

G4 = halo / NH2 / alkylamino <containing 1-6 C> / dialkylamino <each alkyl containing 1-6 C> / CN / alkyl <containing 1-6 C> (substd. by (3) halo) / 16 / OH /

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2463159	AA	20030424	CA 2002-2463159	20021011
BR 2002013239	A	20040928	BR 2002-13239	20021011
EP 1465878	A1	20041013	EP 2002-801341	20021011
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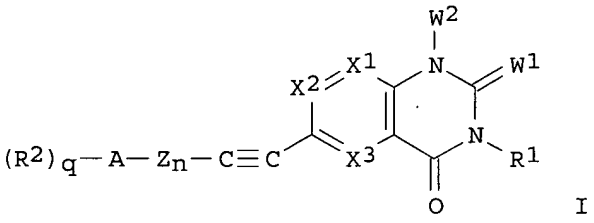
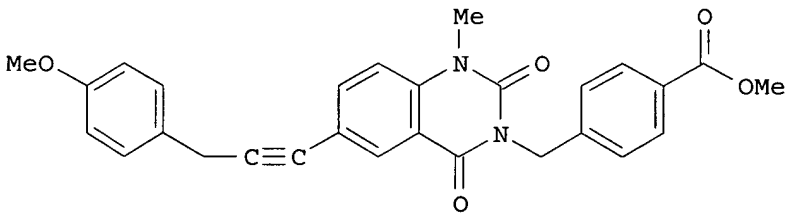
JP 2005509626	T2	20050414	JP 2003-536218	20021011
PRIORITY APPLN. INFO.:			WO 2001-EP11824	20011012
			WO 2002-EP8475	20020712
			WO 2002-EP12194	20021011

GI

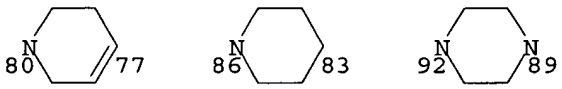


I



II

AB Title compds. I [wherein A = (hetero)aryl or (hetero)cycloalkyl; W1 = O, S, or NR3; W2 = H, CF3, NH2, (di)alkylamino, or (un)substituted (cycloalkyl)alkyl, alkenyl, (hetero)aryl, arylalkyl, or heterocyclylalkyl; or W1W2 = NX4=W3; W3 = N or CR5; X1-X3 = independently N or (un)substituted C; X4 = N or CR7; X5 = O, S, NH, or N-alkyl; X6 = bond, CH2, O, or SO0-2; Z = CR12R13; R1 = H, alkyl, alkenyl, alkynyl, or (un)substituted (hetero)aryl or (hetero)cycloalkyl; R2 = independently H, (trihalo)alkyl, halo, CN, NO2, (CH2)kNR10R11, OR14, SR14, SOR14, SO2R14, acyl, X5(CH2)kNR10R11 (CH2)kSO2NR14R15, X5(CH2)kCO2R14, (CH2)kCO2R14, X5(CH2)kCONR14R15, (CH2)kCONR14R15 X6R16, and trialkylsiloxy; R3 = H, alkyl, OH, or CN; R4 = H or alkyl; R5 = H, OR6, SR6, or (un)substituted (cyclo)alkyl, (hetero)aryl, arylalkyl, or heterocyclylalkyl; R6, R8, and R9 = H or (aryl)alkyl; R7 = H, NR8R9, OR8, SR8, or (un)substituted (cyclo)alkyl, (hetero)aryl, arylalkyl, or heterocyclylalkyl; R10 and R11 = independently H, (hydroxy)alkyl, or arylalkyl; or NR10R11 = (un)substituted heterocyclyl; R12 and R13 = independently H,



G9 = Ph (opt. substd. by 1 or more G10)
G10 = F / Cl / Br / I / NO2 /
alkoxy <containing 1-6 C> (opt. substd. by 1 or more G11) /
alkyl <containing 1-6 C> (opt. substd. by 1 or more G11) /
Ph (opt. substd. by 1 or more alkyl <containing 1-6 C>)
G11 = F / Cl / Br / I
G12 = (1-3) CH2
G13 = O / S / NH
G14 = H / **F** / Cl / Br / I / alkyl <containing 1-6 C> /
alkoxy <containing 1-6 C>
Patent location: claim 1
Note: substitution is restricted
Note: or prodrugs, or salts

L86 ANSWER 17 OF 26 MARPAT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 138:338166 MARPAT
TITLE: Preparation of alkynylated fused ring pyrimidine compounds as matrix metalloprotease 13 inhibitors
INVENTOR(S): Gaudilliere, Bernard; Jacobelli, Henry; Wilson, Michael William; Picard, Joseph Armand
PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033478	A1	20030424	WO 2002-EP12194	20021011
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003033477	A1	20030424	WO 2001-EP11824	20011012
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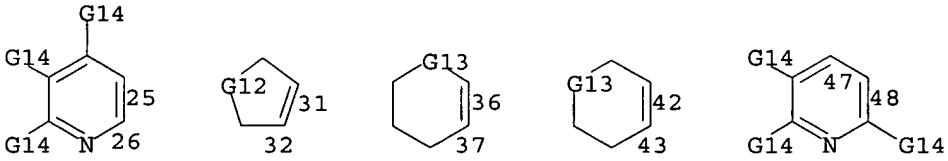
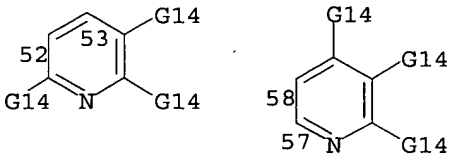
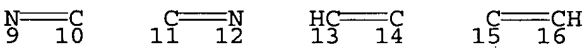
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004007469	A1	20040122	WO 2002-EP8475	20020712
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

zero or more S (no other heteroatoms),
attached through 2 or more C, 1 or more double bonds,
5- to 7-membered monocyclic ring> (opt. substd.) /
25-1 26-3 / **47-1 48-3** / 52-1 53-3 / 57-1 58-3 /
(Specifically claimed: 31-1 32-3 / 36-1 37-3 / 42-1 43-3)

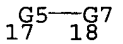




G2 = F / Cl / Br / I / alkyl <containing 1-6 C> /
alkoxy <containing 1-6 C>
G3 = **9-4 10-2 10-7** / 11-4 12-2 11-7 / 13-4 14-2 14-7 /
15-4 16-2 15-7



G4 = alkylene <containing 1-6 C> /
alkenylene <containing 2-6 C> /
cycloalkylene <containing 3-6 C> /
cycloalkenylene <containing 3-6 C> /
heterocycle <containing 1 or more N, zero or more O,
zero or more S, 0 or more double bonds, monocyclic> /
17-3 18-8



G5 = **NH** / 20

G6 = alkyl <containing 1-6 C>
G7 = alkylene <containing 1-6 C> /
alkenylene <containing 2-6 C>
G8 = heterocycle <containing 1 or more N,
zero or more O, zero or more S, attached through 1 or more N>
/ carbocycle / NH / (Specifically claimed: 80-7 77-21 /
86-7 83-21 / 92-7 89-21 / heterocycle <containing 6 atoms,
1-2 heteroatoms, 1-2 N (no other heteroatoms), non-aromatic,
0-1 double bond, 6-membered monocyclic ring>)

PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2474434	AA	20030807	CA 2003-2474434	20030127	
EP 1469854	A1	20041027	EP 2003-703053	20030127	
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US 2005080096	A1	20050414	US 2003-501334	20030127	
JP 2005516053	T2	20050602	JP 2003-563564	20030127	
PRIORITY APPLN. INFO.:			AU 2002-197	20020129	
			WO 2003-JP708	20030127	

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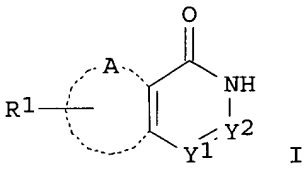
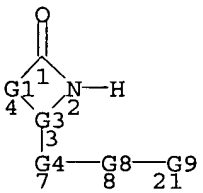


I

AB The title compds. [I; R1 = H, halo, alkyl or alkoxy; A and two adjacent carbon atoms of the six membered ring to be bonded with A form benzene ring, pyridine ring, etc.; Y1:Y2 = N:C(L11R21), C(L12R22):N, CH:C(L13R23), C(L14R24):CH (wherein L11, L12, L13, L14 = alkylene, alkenylene, etc.; R21, R22, R23 and R24 = cyclic amino group, carbocyclic group or amino group which are substituted with (un)substituted Ph); provided that when A and two adjacent carbon atoms of the six membered ring to be bonded with A form benzene ring, then Y1:Y2 = C(L12R22):N, CH:C(L13R23), C(L14R24):CH] having poly(adenosine 5'-diphospho-ribose)polymerase (PARP) inhibitory activity, were prepared Thus, reacting 4-(4-phenyl-3,6-dihydro-1(2H)-pyridyl)butanimidamide with cyclohexanone-2-carboxylic acid Et ester in the presence of K2CO3 in EtOH afforded 2-[3-(4-phenyl-3,6-dihydro-1(2H)-pyridyl)propyl]-5,6,7,8-tetrahydro-4(3H)-quinazolinone which showed IC50 of < 0.5 μM against human PARP.

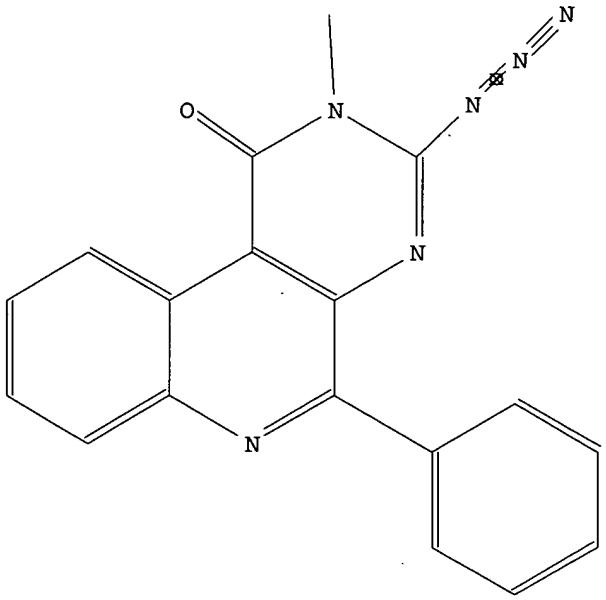
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

MSTR 1



G1 = o-C6H4 (opt. substd. by G2) / carbocycle <containing 5-7 C, attached through 2 or more C, 1 or more double bonds, 5- to 7-membered monocyclic ring> (opt. substd. by G2) / heterocycle <containing 5-7 atoms, zero or more N, zero or more O,

Molecular Weight (MW):	328.33
Lawson Number (LN):	30121, 2817
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	527267
Tautomer ID (TAUTID):	514815
Beilstein Citation (BSO):	5-26
Entry Date (DED):	1988/11/28
Update Date (DUPD):	1992/01/31



Field Availability:

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CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	2
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
BSO	Beilstein Citation	1
DED	Entry Date	1
DUPD	Update Date	1
MP	Melting Point	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1

RXPRO Substance is Reaction Product 1

All References:
ALLREF

1. Lalezari; Sadeghi-Milani, J.Heterocycl.Chem., CODEN: JHTCAD, 16, <1979>, 707,708

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